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ABSTRACT

Nutrition is well-recognized as a necessary component of educational programs for physicians. This is to be valued in that of all factors affecting health in the United States, none is more important than nutrition. This can be argued from various perspectives, including health promotion, disease prevention, and therapeutic management. In all cases, serious consideration of nutrition related issues in the practice is seen to be one means to achieve cost-effective medical care. These modules were developed to provide more practical knowledge for health care providers, and in particular primary care physicians. The purpose of this module is to instruct the primary care physician in the determination of the role nutrition plays in the etiology and treatment of behavioral and neurological disorders. Diet and the nutritional status of the individual are related to behavior during various stages of the life cycle and under a variety of conditions. Included are learning goals and objectives, a self-check of achievement with regard to goals, resources for physicians and 117 references. Appendices include tables of health problems and associated risk factors, nutritional assessment and intervention guidelines, federally sponsored food assistance programs, and self-help groups and national treatment centers for eating disorders. (CW)

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25. **Preventing Hospital and Home Malnutrition**
26. **Questions About Common Ailments**

Faculty Guide (includes comprehensive index for Modules 1-26)

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Introduction

"A few quick drinks late in pregnancy can damage the fetal brain"
"Starving for Attention - Sherry Boone's True Life Story"
"People who crave sugar and carbohydrates are merely seeking a natural high"
"Diet and vitamin supplementation can cure schizophrenia"
"Sugar causes hyperactivity in children"

These are only a few of the headlines seen recently in the popular press. All relate in one way or another to the current research and popular interest in the role of nutrition in human behavior. This area encompasses a wide range of research interests including:

1. the large body of data on effects of malnutrition on fetal and childhood growth and development (including intelligence and behavior);
2. the effects of ethanol and drug use on the developing fetus, as well as the user;
3. the growing problem of anorexia nervosa and bulimia;
4. the role of diet in the synthesis of brain neurotransmitters and how this translates into human behavior; and
5. the promotion of nutritional and orthomolecular therapies for mental illness, schizophrenia, depression, pre-menstrual syndrome (PMS), mental retardation, hyperactivity or attention deficit disorder, and even antisocial and criminal behavior.

As a primary care physician, you are often faced with answering patients' questions and providing advice on these widely publicized topics, often long before conclusive research data are available. The purpose of this module is to help you determine what role, if any, nutrition plays in the etiology and treatment of these conditions and how to apply the best available and reliable data to this treatment.

Since it is impossible to cover each area in depth, appropriate references and review articles are suggested for further reading. Community agencies, programs, and resources are included, where appropriate, so that the physician and patient can take full advantage of all avenues of therapy.

Goal

The goal of this module is to review how diet and the nutritional status of the individual affect behavior during various stages of the life cycle and under a variety of conditions.

Objectives

Upon completion of this module, you will be able to:

1. *Describe normal neurological growth and development and discuss the impact of malnutrition on growth and behavior.*
2. *Identify women at risk for delivering small-for-gestational-age infants and discuss methods for assessing, monitoring, and reducing this risk in a practice population.*
3. *Outline the research on the effects of diet on brain neurotransmitter levels and discuss the potential impact on human behavior and disease treatment.*
4. *Recognize the features of fetal alcohol syndrome and discuss methods of prevention.*

5. *Recommend to pregnant patients the most appropriate diet and health habits for the optimal growth and development of their babies.*
6. *Outline the criteria for the diagnosis of anorexia nervosa and bulimia and discuss appropriate treatment approaches, including nutritional rehabilitation.*
7. *Describe the behavior syndromes of pre-menstrual syndrome, reactive hypoglycemia, attention deficit disorder, and schizophrenia popularized by the media to be related to nutrition, and recommend to patients the most appropriate nutritional programs based on reliable research data.*

Normal Growth, Development, and Metabolism

Much has been learned in recent years about brain cell proliferation and specialization. Brain growth involves the development of essentially two populations of cells, neurons and glial cells, which have differing growth periods. The neurons grow from the end of the first trimester of pregnancy until the 25th week. The one-pound neonate brain contains an estimated 100 billion neurons, essentially the same as that found in the three-pound adult brain.[1,2] The glial cells proliferate at the 23rd gestational week, peak at birth, and decline during the third postnatal month. Glial cell division occurs at a reduced rate until the child is two to three years old; cell number is estimated to be 10 times that of the neurons, and they constitute one-half of the mass of the brain.[2] Once the process of brain growth is completed at around 2½ to 3 years of age, no matter what is affecting the child, the process cannot be initiated again.

The concept of "critical time period" in brain development has received considerable attention in the past 50 years, and refers to a rapid period of development that cannot occur at a later time period. The "critical period" in human brain development varies for various brain sub-parts but comes postnatally between early fetal life and the fourth year. Neuronal cells form primarily *in utero*, glial cells form within the first year of life, and myelin accumulates primarily in the second postnatal year of the human. An insult during any one of these periods of development may affect one brain parameter more than another.[3] Table 24-1 outlines the normal brain development of the fetus.

The neurons are considered responsible for human thought processes. The more complex the neural circuitry or the more connections made between neurons, theoretically the greater the potential for learning. Most neurons are located in the cerebrum. They have a finite lifespan and when they die, they are replaced by glial cells.

Skim milk is not recommended for infants' diets because it is deficient in essential fatty acids and low in total energy. Human milk or appropriate infant formulas are the recommended sources of nutrition during the first year of life.

Glial cells are satellite cells for neurons. They do not conduct an electrical impulse but rather form a trellis-like support structure upon which the neuronal bed lies. There are two types of glial cells: the oligodendrocyte and the astrocyte. The oligodendrocytes predominate in white matter, where they form myelin around large neuronal axons. Lipids accumulate as myelin is synthe-

Table 24-1. Calendar of Normal Brain and Behavioral Development

Embryo		Fetus	
3 weeks	- neural plate begins to fold	10 weeks	- electrical impulses detected in reticular activating system
4 weeks	- neural plate completes fold into neural tube; nerve-cell proliferation inside tube begins	12 weeks	- face and hand movements begin
		3-5 months	- nerve cell proliferation occurs in cerebral hemispheres, peaking at 26 weeks
4½ weeks	- neuroblasts migrate; axons grow from neuroblasts; hemisphere first delineated; optic vesicles appear	5th month to 3 months postnatal	- glial cell proliferation begins in the cerebral hemisphere, peaking at birth; myelination of axons and dendritic arborization begins
		7½ months	- fetus places hands to mouth; sucks on them; eyeballs open

From Filer, L.J. (ed.): *The Brain*. Lyndhurst, N.J.: Health Learning Systems, Inc., 1982, Chapter 5, p.8. Used with permission of the publisher.

sized. By age two or three, 90% of total lipid accumulation in the brain has taken place.[2] Myelination is important for enhancement of nerve transmission. Lipids account for 75% of human myelin, with cholesterol being the major component; proteins account for the remainder of myelin. If there is insufficient fat in the diet, it is believed that lipid synthesis, especially cholesterol, will be impaired. This could lead to impaired myelination and behavioral deficit.[4] Also, essential fatty acids are precursors of prostaglandins which are important neuromodulators. This is why skim milk, or even 1% milk, which is low in both energy and essential fatty acids, is not recommended for infants' diets and why human milk or appropriate infant formulas are the recommended sources of nutrition during the first year of life. Approximately 30 to 50% of total kilocalories for the infant should be supplied by fat, with three to four percent of this provided in the form of linoleic acid.

Glycolipids and Glycoproteins

Early myelination, dendritic arborization, and synaptic transmission all depend upon sufficient amounts of glycolipids and glycoproteins in the brain. All milk contains glycoproteins, with human milk having the highest concentration. Glycolipids appear to be important in central nervous system metabolism and glycoproteins in peripheral nervous system myelination.[5] Cerebrosides and gangliosides are the two brain glycolipids. Laboratory animals seriously malnourished during maximum brain growth show immature spectra of gangliosides.

Brain Neurotransmitters: Diet and Human Behavior

Neurotransmitters are chemical substances manufactured by neurons from precursor molecules inside axons. The nerve cell membrane across the synapse from the axonal terminal has receptor sites for the particular neurotransmitter. There may be thousands of synaptic vesicles in a single terminal, each of which contains between 10,000 and 100,000 molecules of the transmitter.[2,6] Messages to neurons can be either excitatory or inhibitory. Neurotransmitters in the brain are dopamine, norepinephrine, serotonin (5-hydroxy-tryptophan), acetylcholine, gamma-aminobutyric acid (GABA), glycine, the acidic amino acids glutamate and aspartate, epinephrine, and perhaps some peptides.[7] There is growing evidence that neurotransmitters may play a role in the control of the proliferation and possibly the differentiation of young nerves.

Much has been written in the scientific literature and popular press in recent years about the effect of diet on the synthesis of brain neurotransmitters; a popular book, *The Carbohydrate Craver's Diet*,[8] has evolved from research in the area. Unfortunately, as with all newly investigated areas, claims have been made that exceed any of the reliable data. Once the media popularize a concept, fiction and unproven theories are often accepted as fact, and treatment programs are developed and implemented based on unproved premises. Obviously, the nutrition of the human is only one of many complex factors that affect overall behavior, and it is simplistic in most instances to attribute particular behavior patterns solely to diet or a component in food.

Brain neurotransmitter function may not be as autonomous as previously believed. Although highly debatable and with very limited support, normal fluctuations in the dietary availability of tryptophan, tyrosine, or choline may exert an influence on the rate of neuronal synthesis of serotonin, catecholamines, and acetylcholine, respectively.

It was once believed that cerebral metabolism was carefully controlled and regulated via the blood/brain barrier and that dietary sources of energy were relatively unimportant for brain function on a short-term basis. It now appears that brain neurotransmitter function may not be as autonomous as previously believed. Although highly debatable and with very limited support, normal fluctuation in the rate of availability of tryptophan, tyrosine, or choline following food consumption may exert an influence on the rates at which neurons synthesize serotonin, catecholamines, and acetylcholine, respectively.[9] This purportedly occurs because the amino acid and choline composition of the plasma may be altered by the diet, which causes parallel changes in precursor availability to the blood brain barrier and for neurotransmitter synthesis. It is debatable, however, that such small amounts of these dietary substrates could affect neurotransmitter synthesis in the adult brain.

Dietary Control of Serotonin Synthesis

Tryptophan, an essential amino acid, is a precursor for brain serotonin synthesis. Tryptophan is transported into the brain via a carrier system shared with other large

neutral amino acids (valine, leucine, isoleucine, methionine, phenylalanine, and tyrosine).[9-11] Some limited research has shown that the amount of tryptophan available to the brain may control serotonin synthesis and that brain tryptophan may be regulated by three factors: (a) plasma tryptophan levels, (b) nutritional state, and (c) plasma concentration of other large neutral amino acids.[12-14]

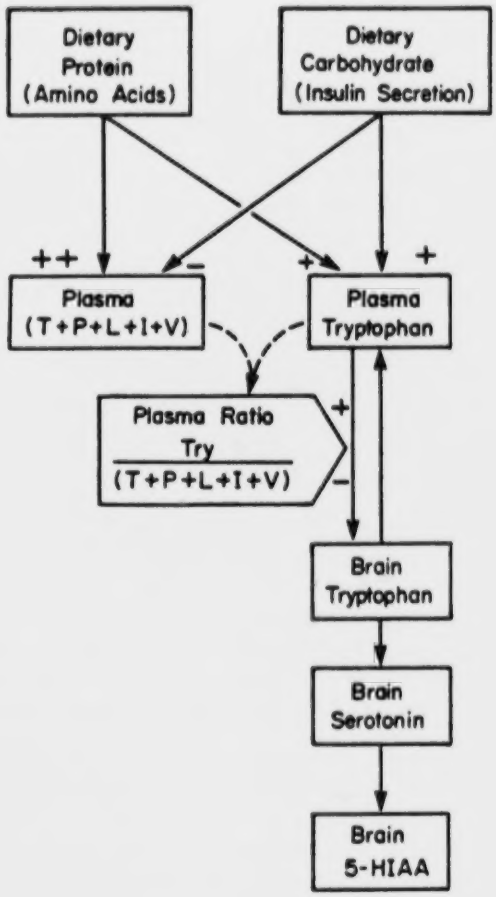
Rats injected with small doses of tryptophan demonstrate increased plasma and brain tryptophan levels and increased brain serotonin levels. The increase in serotonin synthesis appears to be due to increased synthesis, not decreased catabolism. Tryptophan hydroxylase, the rate-limiting enzyme in serotonin synthesis, appears not to be saturated at physiological levels of tryptophan, and hence increases in substrate result in increased neurotransmitter synthesis (Figure 24-1).

Insulin, which is elevated after a high carbohydrate meal, may elevate plasma and brain tryptophan levels and enhance serotonin synthesis.[9]

Brain tryptophan content depends on the ratio of plasma concentration of tryptophan to the sum of the concentrations of other large neutral amino acids that compete with tryptophan for transport into the brain.

Although injection of tryptophan raises serum levels, a high-protein meal (18-24% of total kilocalories) does not raise brain levels or increase neurotransmitter synthesis. Brain tryptophan content in the intact normal animal depends on the ratio of the plasma concentration of tryptophan to the sum of the concentrations of other large neutral amino acids that compete with tryptophan for transport into the brain.[9] Most protein foods contain relatively small amounts of tryptophan (0.8 to 1.5%) and larger proportions of other amino acids. Since the same system that carries tryptophan from plasma into the brain also transports other large neutral amino acids, a high-protein meal retards the uptake of tryptophan into the brain by disproportionately increasing the concentration of other amino acids that compete with tryptophan (Figure 24-1).

Figure 24-1. Hypothesized Model to Describe Diet-Induced Changes in Serotonin Synthesis in the Brain



The ratio of tryptophan to the sum of other large neutral amino acids [i.e., tyrosine (T) + phenylalanine (P) + leucine (L) + isoleucine (I) + valine (V)] in blood is thought to control tryptophan uptake into brain and brain tryptophan concentration.

Fernstrom, J.D., and Wurtman, R.J.: "Brain Serotonin Content: Physiological Regulation by Plasma Neutral Amino Acids." *Science*, 178:414-416, p. 416, 1972. Used with permission of the publisher.

Treatments that increase brain serotonin levels may enhance serotonin release as well. It is difficult to directly measure neurotransmitter release from the central nervous system of animals, and measurement has not been done in humans.[9] Lytle, et al., found that low-tryptophan diets reduced brain serotonin levels in rats and lowered the threshold to noxious stimuli; this effect was reversed by adding adequate tryptophan to the diet.[15]

Diet and Brain Catecholamine Synthesis

Tyrosine is the amino acid precursor of dopamine and norepinephrine. Brain tyrosine is derived either from dietary tyrosine or from phenylalanine, which is converted to tyrosine in the liver. Plasma tyrosine levels fluctuate during the day, as do those of tryptophan, and tyrosine enters the brain by the same low-affinity, unsaturated uptake mechanism as that for tryptophan.[9] The enzymes which convert tyrosine to dopamine (tyrosine hydroxylase) and dopamine to norepinephrine (dopamine-B oxidase) are not fully saturated *in vivo*. Increasing tyrosine can increase rates of conversion to dopamine and/or norepinephrine.

The synthesis of dopamine from tyrosine appears to become precursor-dependent only when dopaminergic neurons increase their firing rate. Some studies suggest that increased blood tyrosine may accelerate norepinephrine synthesis and release, even in the absence of neuronal activation.

Unlike tryptophan, increased serum tyrosine does not elevate brain dopamine or norepinephrine levels. Tyrosine hydroxylase appears to become precursor-dependent only when dopaminergic neurons increase their firing rate.[9] Treatments that accelerate the firing rate of dopaminergic neurons may activate the enzyme and amplify its dependence on tyrosine levels.[16] Little information, however, is available at present concerning the functional consequences or precursor-induced changes in brain catecholamine synthesis.

Dietary Intake of Choline and Brain Acetylcholine Synthesis

The synthesis of acetylcholine is dependent upon the availability of its precursor, choline, which comes primarily from liver synthesis.

The synthesis of acetylcholine, the brain neurotransmitter synthesized from choline, is also precursor-dependent, since its control enzyme, choline acyltransferase, is not saturated under physiological conditions *in vivo*.[9] The brain cannot synthesize choline *de novo* and must obtain it from blood circulation.[17] Blood choline comes primarily from liver synthesis of phosphatidyl choline (lecithin); a small amount may come from the diet. Choline is a natural dietary constituent covalently bound to glycerol and fatty acids in the form of lecithin. Eggs, meat, fish, and legumes are good dietary sources of lecithin. Humans generally ingest 1 gm of choline per day as part of common foods, usually in the form of lecithin. Choline uptake and synthesis are also controlled by substrate inhibition, so when plasma choline levels rise, so do brain levels, and hence acetylcholine synthesis.[18] Choline administration may enhance release of epinephrine from the adrenal medulla.[9]

Clinical Application of Precursor Therapy

Although not well researched, the above observations suggest that certain central nervous system disorders and physiological conditions, such as hepatic coma, might be treated by dietary means or through pharmacological doses of tryptophan, tyrosine, and choline (or lecithin).

Dietary treatments that increase brain serotonin levels have been used to treat patients whose disease states result from presumed deficiencies of serotonergic transmission, including the primary affective disorders, schizophrenias, myoclonias, Parkinson's disease, migraine headache, Lesch-Nyhan syndrome, and insomnia or decrease in sleep latency.[10] Serotonergic pathways are felt to influence many biological systems, including sleep, temperature regulation, pain, mood, and aggressive behavior.[9,19]

It is not within the scope of this module to describe and evaluate all the research on neurotransmitter percursor therapy. Recommended sources are provided in the Resources for Physicians for more in-depth coverage. In the following paragraphs, however, promising research will be highlighted, problems with research to date and some conclusions will be discussed, and implications for future research and therapeutic application will be outlined.

The use of precursor therapy for treatment of the primary affective disorders of depression and mania is

based on the biogenic amine theory of primary affective disorders.[20] This theory postulates that central nervous system deficiencies of norepinephrine and/or serotonin are causally related to depression and that excessive norepinephrine release may underlie mania.[21]

It has been suggested that some individuals suffer from depression because of a functional deficit of brain norepinephrine and/or serotonin activity.

Since the MAO (monoamine oxidase) inhibitor class of antidepressants results in the reduction of catabolism of serotonin and norepinephrine, and since most tricyclic antidepressants also enhance brain activity of one or both of these monoamines, it has been suggested that some individuals are depressed because of a functional deficit of brain norepinephrine and/or serotonin activity.

Studies on the use of tyrosine in depression are limited. In a few double-blind studies done with very small numbers of patients, some individuals did show improvement with tyrosine therapy as compared to placebo, but more research needs to be conducted with this amino acid precursor. Tyrosine has been shown to lower blood pressure in rats, and tyrosine availability in the brain has been purported to influence the rate at which nerves synthesize dopamine and norepinephrine.[9]

Large intakes of tryptophan or tyrosine, or a high-protein meal, could possibly inhibit the uptake and effectiveness of l-dopa and methyldopa due to competitive uptake at the blood brain barrier.

L-dopa, a biochemical product of tyrosine hydoxylation and an intermediary in dopamine synthesis, has been used successfully to treat Parkinson's Disease. Since l-dopa and methyldopa, an antihypertensive agent, compete with large neutral amino acids for uptake at the blood brain barrier, large intakes of tryptophan or tyrosine or a high-protein meal could theoretically inhibit the uptake and effectiveness of these medications. To maximize the efficacy of these drugs, the physician prescribing them should advise the patient to take the drug between meals or with dietary carbohydrates that would enhance insulin secretion and lower large neutral amino acids in the blood. The physician should also advise a general reduction in dietary protein intake if the patient is consuming a high-protein diet.[12]

Serotonin Precursor Therapy

There is possibly a "therapeutic window" of optimum tryptophan effectiveness in the treatment of depression, with greater effectiveness at doses of 3 to 6 gm/day.

Reports on the efficacy of tryptophan in treating depression are conflicting, and its use remains controversial. In most studies, researchers did not attempt to control the consumption of other relevant dietary constituents or to utilize a double-blind crossover design. Studies using the double-blind technique indicate that there is possibly a "therapeutic window" of optimum tryptophan effectiveness in the treatment of depression, with maximal effectiveness at doses of 3 to 6 gm/day (the average daily intake of tryptophan is 1 to 1.5 gm/day). Studies using higher doses (up to 12 gm/day) showed tryptophan to be less effective and possibly harmful.[22]

Clinical Implications for the Primary Care Physician

Although use of tyrosine and tryptophan as antidepressants is a therapeutic possibility, the primary care physician needs to be aware that supplementation of free amino acids can cause amino acid imbalances and toxicity. Little is known about the long-term side effects of this therapy.

Although use of tyrosine and tryptophan as antidepressants or as adjunctive antidepressive agents is a therapeutic possibility, advising patients to eat a high-protein diet will not accomplish this end because of competitive inhibition of large neutral amino acids in the diet. Use of free amino acids should be more effective in raising brain levels, but free amino acid supplementation can cause more side effects than food and result in amino acid imbalances and toxicity. Little is known about the long-term effects of even moderate changes in amino

acid balance or about the interaction of amino acids with conventional drugs. Also, there is no way at this time to distinguish between those depressed patients who would be likely to respond to tyrosine or tryptophan and those patients whose depression is unrelated to either of these precursors.

Tryptophan has been used successfully to suppress involuntary muscular contraction in some patients with post-hypoxic intention myoclonus, following cardiac arrest.[9] Tryptophan has also been used to treat various sleep disorders.

There is abundant evidence that serotonergic neurons do participate in normal sleep. Doses of precursors such as tryptophan may have some therapeutic utility.

Even though it is unlikely that a single set of neurons "controls" sleep, there is abundant evidence that serotonergic neurons do participate in normal sleep, and doses of precursors may have some therapeutic utility. Single oral doses of tryptophan of 5 to 10 gm, given at bedtime, increased total sleep time and decreased the number of nocturnal awakenings in some patients with insomnia.[9] It is possible that tryptophan itself may act as a sedative independent of its effect on serotonin levels. It has been hypothesized that tryptophan therapy would be most effective when combining it with sugar to increase the insulin response and with tyrosine to suppress the reduction in brain catecholamine synthesis, but this has not been fully tested at this time.

The few reports on administration of serotonin precursors for treatment of schizophrenia did not show any significant improvement in signs or symptoms. Researchers at McGill University have investigated tryptophan supplements (4 to 8 gm/day) to treat aggressive behavior in schizophrenia and as an adjunct to lithium carbonate in the treatment of manic-depression.[23] Preliminary results from a small number of patients are promising, and research using larger numbers of patients is underway.

The theory behind the carbohydrate craver's diet is that hunger for carbohydrates leads to carbohydrate feeding and carbohydrate ingestion causes serotonin levels to rise, which decreases hunger and enhances feelings of well-being.

Serotonergic neurons may affect appetite and influence food choice since they apparently monitor changes in blood amino acid composition. In experimental animals, for example, therapy that increases serotonin transmission suppressed carbohydrate but not protein consumption. This is the premise upon which the Carbohydrate Craver's Diet is based.[8,24]

Essentially the theory is that hunger for carbohydrates leads to carbohydrate feeding, and carbohydrate ingestion causes serotonin levels to rise, decreasing the hunger feeling and enhancing feelings of well-being. It is hypothesized that there is a sub-group of individuals who are carbohydrate cravers, who have a biological craving for sugars and starches, and who consume a substantial portion of their daily caloric intake as sweet or starchy snacks. However, current research data on human subjects are insufficient to support this hypothesis or warrant promotion of a particular diet for the general public. There is, however, a good possibility that appetite is *in part* regulated through serotonin and other neurotransmitter mechanisms. Also, the recommendation to dieters to include carbohydrate foods as part of the daily food intake and to avoid high-protein/low-carbohydrate diets is sound advice in order to avoid "binge" or compulsive eating. However, more research in human subjects of this hypothesis for appetite control needs to be completed before specific advice should be given to the obese or weight-conscious public.

Clinical Use of Choline and Lecithin

Tardive dyskinesia, characterized by involuntary tongue, lip, and jaw movements, occurs frequently in people who take antipsychotic drugs. Large doses of choline chloride (up to 25 gm/day) have been found to suppress these movements in some patients.[25] Choline is also being investigated to treat the memory loss and dementia of Alzheimer's disease, in which cholinergic neurons are selectively damaged. The level of choline acyltransferase, the enzyme which catalyzes the conversion of choline to acetylcholine, is selectively reduced in the brain cortex and caudate nucleus of people with Alzheimer's disease.[9]

Lecithin is preferred by some researchers as a source of choline since it produces prolonged elevations of plasma

choline levels and does not result in a fishy odor from the patient's breath, sweat, and urine that is caused by choline. The doses of lecithin depend on its phosphatidyl choline content. Most commercially available lecithin (including "pure" lecithin) contains only 15 to 30% phosphatidyl choline, and, as a result, patients must take 50-100 gm/day to increase plasma choline levels significantly. Diet is therefore a poor source and presumably should have no effect on plasma choline levels. In contrast, 10 to 15 gm/day would be sufficient if phosphatidyl choline were the only phospholipid in the lecithin compound.

The popular press has publicized the possible role of cholinergic neurons for normal memory. Therefore, some individuals have promoted dietary lecithin as a means of improving memory and preventing dementia.

The popular press has picked up on the hypothesis that cholinergic mechanisms may be important for normal memory and hence has promoted the ingestion of choline and lecithin to improve memory in normal humans.

Sitaram, et al., found that single doses of acetylcholine or of choline enhanced serial learning in normal individuals.[26] More research needs to be conducted in this complex and multifactorial area of human behavior before choline can be recommended as a dietary enhancement of human memory.

Summary

The brain neurotransmitters, serotonin, epinephrine, norepinephrine, and acetylcholine, are synthesized in the neurons from the precursor substances tryptophan, tyrosine, and choline (lecithin), respectively. It appears that under various circumstances synthesis of these neurotransmitters may be affected by the availability and uptake of these precursors. The amount of available precursor in the plasma varies according to the particular composition of a meal (high-carbohydrate versus high-protein) or through the use of synthetic diet mixtures.

These observations have led researchers to investigate the use of "dietary" neurotransmitter precursor therapy to treat a variety of neurologic and psychiatric disorders. It must be emphasized that much of this treatment to date is not dietary manipulation *per se*, other than encouraging higher-carbohydrate and lower-protein intakes to facilitate precursor uptake. Very large doses of any of these compounds have usually been employed in research protocols so that the compound is utilized as a drug, not a nutrient. Also, there is no evidence to suggest that any of the neurological disorders under treatment are caused by a deficiency of tryptophan, tyrosine, choline, or lecithin.

The investigation of neurotransmitter precursor therapy will continue to expand and may result in exciting and effective treatments for a variety of neurological problems. However, present research is primarily experimental and should not be recommended by the practicing physician.

Clinical studies have been conducted using tryptophan, either alone or in combination with other therapies, to treat a variety of psychiatric and neurologic diseases, including recurrent pain following rhizotomy and cordotomy, depression, myoclonias, and insomnia.[22] Tyrosine may prove beneficial in treatment of depressive disorders, Parkinson's disease, and hypertension, although limited research has been done to date. Choline or lecithin may benefit patients suffering from tardive dyskinesia and Alzheimer's disease and may have a relationship with human memory processes.[27] It is anticipated that investigation of neurotransmitter precursor therapy will continue to expand and may result in exciting and effective treatments for some very difficult and frustrating neurological problems. However, the research is still in the experimental realm, and at this time such therapy should not be recommended by the practicing physician. In the meantime, the physician needs to inform patients who inquire about these therapies about their experimental nature and warn them of the hazards of self-imposed therapies which could result in potentially harmful amino acid imbalances.

Fetal and Infant Undernutrition: Effects on Intellectual Development and Behavior

Effects of undernutrition on the intellectual development and behavior of the individual are still controversial. Intelligence is difficult to define and measure; it is influenced by the

maturation and attention span of the child, which seemingly can be altered by undernutrition.

Fetal and early childhood undernutrition plays a demonstrable part, interdependently with a host of other environmental factors, in permanently reducing many persons' achievements to levels below the naturally endowed potential. In developed countries, such as the U.S.A., parental neglect, child abuse, and failure to thrive are the most common causes of undernutrition.

The effects of undernutrition on the intellectual development and behavior of the individual are still controversial, despite extensive research over the past two decades. Many difficulties in the interpretation of this research stem from trying to apply results from animal research to humans and in determining the critical periods of brain growth and development when the insult occurs.

Intelligence is difficult to define and measure and is influenced by variables such as motivation and attention span, which are possibly altered in previously undernourished children. Malnourished infants are lethargic and listless; they withdraw from their environment; they have a lower, less demanding cry; and they receive little in the way of social interaction. In this respect, the effects of malnutrition contribute to the lack of environmental stimulation necessary for the development of intelligence. It is not known which factors in the brain are important in intelligence.

Many biochemical and structural alterations can be associated with impaired brain function; i.e.,

loss of certain types or numbers of brain cells,
impaired myelin formation,
altered protein synthesis,
altered glycosaminoglycan (mucopolysaccharide) formation,
decreased cell size or number of axon-dendrite connections, and
impaired formation of neurotransmitters.[13]

Prenatal Undernutrition in Humans: Intrauterine Malnutrition

An extremely high percentage of infants born in developing countries and in poorer sections of developed countries, including the United States, weigh less than 2500 gm (5.5 lb). In developing countries and some segments of developed countries, more than 50% of low-birth-weight infants are undergrown rather than premature. This frequency can constitute from 15-20% of the entire world's newborn population. There are 300 million people in the world today who undergo significant amounts of undernutrition during early life.

The concept of the fetus as the "perfect parasite" extracting all essential nutrients at the expense of the maternal stores has been replaced with the understanding that the fetus is vulnerable to a variety of maternal influences, including nutrition.

Studies in laboratory animals and the effects of wartime famines have indicated that the human fetus is vulnerable to several nutrient deprivations. Less information is available concerning the consequences of more subtle nutritional deficiencies. The manifestation of diminished nutritional support for the fetus *in utero* is delivery of a full-term, low-birth-weight infant, also called small-for-gestational-age. Other causes for birth of small-for-gestational-age infants are placental insufficiency, high-altitude living, intrauterine infection, maternal smoking, and chromosome defects. Such infants are at risk for higher mortality, greater postnatal complications, and a higher incidence of mental/motor retardation at a later age.[11]

Small-for-gestational-age infants can result from undernutrition if the mother's maternal stores are depleted because of inadequate food intake, maternal illness, or frequent and close pregnancies.

As a primary care physician, especially one involved in prenatal and postnatal care, knowledge of mothers at risk for small-for-gestational-age infants and methods of diagnosis and intervention are important. Small-for-gestational-age babies can result from undernutrition (a) as the mother's maternal stores are depleted, which may occur when past and present maternal food intake is inadequate; (b) as a result of maternal illness; or (c) as a result of frequent and close pregnancies. As the ability to identify potential intrauterine malnutrition improves,

we will better be able to nurture the fetus *in utero*, such as via the amniotic fluid.

Pregnancies complicated by intrauterine growth retardation are associated with a 6- to 8-fold increase in infant mortality and morbidity. Intrauterine growth retardation is demonstrated in 10% of perinatal deaths. Long-term changes in neurological and intellectual development are difficult to assess, but school performance tends to be below normal in intrauterine growth retardation children, even for those who did not have neonatal asphyxia and hypoglycemia.[28]

Biochemical analyses of brains from infants suffering from both intrauterine and postnatal undernutrition have demonstrated alterations in quantities of brain cells, myelin lipid, total brain protein, and brain glycosaminoglycans. The degree of reduction of these substances is related to the timing of the undernutrition as well as the severity. With adequate postnatal nutritional rehabilitation, it is likely that recovery of brain cell numbers might occur during the period of postnatal cell division, but there are insufficient data to date on the effect of rehabilitation on the human brain. Analyses have not been performed on the brains from small-for-gestational-age infants who have periods of normal growth after birth or on previously postnatally undernourished infants who undergo rehabilitation. The effect of undernutrition on the developing brain seems to provide permanent deficits of some relevant structures, not because they have been damaged or destroyed, but because they have simply failed to arrive at sufficient numbers at the correct time.[29]

Undernutrition and Higher Mental Function

In one of the best studies of the effects of early and late malnutrition on intellectual performance, Winick, et al., found that severely malnourished Korean infant girls who were adopted by U.S. families after age 2 and had complete nutritional rehabilitation did not reach American average scores for I.Q. and achievement. In contrast those Korean infants who were moderately or well-nourished scored higher than American children.[30] In this case, nutritional status was found to have a profound effect on achievement, and environmental stimulus could not compensate completely for the deficit.

However, a separate study of children who were adopted earlier, before the end of the brain growth period (ages 1½ to 2 years), showed that after 6 years in the U.S. severely undernourished, moderately undernourished, and well-nourished children had I.Q. and achievement scores surpassing not only the average Korean child, but also those of the average American child. The severely malnourished girls (below the third percentile) still performed less well than the moderately nourished and well-nourished children.[31]

In these cases, environmental stimulation seems to have partly overcome even the effects of severe malnutrition. Therefore, if nutritional rehabilitation and environmental stimulation are initiated before the end of the brain growth period (i.e., before age 2) there is hope for excellent recovery, even from severe malnutrition, at least in respect to the parameters we are able to measure. None of this research detracts from the importance of nutrition for the development of intellect. It merely places nutrition in a setting along with many other equally important contributors to the performance outcome. Reference #3 in the Resources for Physicians provides an excellent review of nutritional rehabilitation protocol for the malnourished infant and child.

Undernutrition and Body Structure as it Relates to Brain Development

There is emerging evidence that body stature achievement can be restricted by undernutrition at the time of the brain growth spurt and that such stunting may not be fully compensated by catch-up growth via nutritional rehabilitation.[32] Contrary to the popular cell number/cell size hypothesis of the 1960's and 1970's, it is now recognized that tissues and organs do not pass through two phases of cell development; i.e., cell hyperplasia followed by cell hypertrophy. Rather, mean adult cell size is achieved first, with cell number continuing to increase as long as growth itself persists into adulthood.[33]

Brain growth is closely linked with body growth. Therefore, health professionals should promote optimum somatic growth in the period after birth and before the second or third birthday.

Brain growth is indissolubly linked to body growth. Therefore, the promotion of the best somatic growth in the period after birth and before the second or third birthday is the best we can do to ensure good brain growth. In fact, a slight excess of intake is to be preferred to infant undernutrition.[29] These recommendations do not conflict with present principles of child feeding which discourage early introduction of solid foods and

the forced feeding of infants in spite of indications of fullness. Letting the child dictate food amounts is probably the best advice for parents, along with close monitoring of linear growth and body weight.

Nutritional Guidelines for Pregnancy

For a more detailed discussion of nutritional needs during pregnancy, please refer to Module 7, Normal Diet: Pregnancy and Lactation. In general, a nutritionally balanced diet that meets the increased energy requirement of the pregnant woman can provide all of the necessary nutrients in adequate amounts except for iron and folacin. Consequently, dietary supplementation with iron (30-60 mg of elemental iron) is recommended to prevent depletion of maternal iron stores and iron deficiency anemia. Low serum folacin levels are more often observed in pregnant women. The significance of this is unknown since megaloblastic anemia is uncommon in the U.S. Routine supplementation with folacin (200-400 μg/day) is still a controversial issue.[34] Diet supplementation is reasonable for the high-risk pregnant woman with a history of poor dietary intake, frequent or multiple pregnancies, chronic hemolytic anemia, or if receiving anticonvulsant therapy.

Pre-pregnancy weight is an important variable in considering energy needs in pregnancy. The optimal weight gains recommended for pregnant women are 30 pounds for underweight women, 20 pounds for normal weight women, and 16 pounds for women overweight at the start of pregnancy.

Energy needs are increased during pregnancy by 300 kcal/day in the second and third trimester, or about 15% above the non-pregnancy state.[35,36] A weight gain of at least 24 to 27 pounds during pregnancy is associated with the best reproductive performance and lowest perinatal mortality rates.[37] Maternal nutrition reserves are an important determinant of optimal weight gain during pregnancy. Naeye, after examining the records of 44,568 normal and abnormal pregnancies, determined that maternal energy intake had the largest influence on pregnancy weight gain. The optimal weight gain (i.e., lowest perinatal morbidity rates) was 30 pounds for underweight women, 20 pounds for normally proportioned women, and 16 pounds for women who were overweight at the start of pregnancy.[38] Thus for the primary care physician, pre-pregnancy weight is an important variable in considering energy needs during pregnancy.

Although the optimal weight gain for overweight mothers appears to be one-half that for underweight mothers, pregnant women should not be advised to unduly restrict energy intake during pregnancy. The finding that overweight mothers who gained the least amount of weight had twice the perinatal mortality, as compared to overweight mothers with large weight gains, emphasizes the inherent dangers of inadequate weight gain during pregnancy, even for overweight mothers.

The patterns of weight gain during pregnancy may be more important than the total weight gain. The usual pattern consists of minimal gain during the first trimester followed by a progressive linear rise during the second and third trimesters.

Population studies indicate that the most important factors predicting infant size at birth are the gestational age of the infant, followed by maternal pre-pregnancy weight and weight gain during pregnancy.[35] Women who enter pregnancy with a low pre-pregnancy weight and who restrict their weight gain during pregnancy are at increased risk of delivering low-birth-weight infants, as compared with heavier mothers who have higher weight gains.[38,39]

Maternal diets low in energy intake are likely to be deficient in essential nutrients important for placental and fetal development, such as protein, vitamins, and minerals.

Diets low in energy intake (i.e., less than 1600 kcal) are likely to be deficient in essential nutrients important for placental and fetal development. Protein may be diverted for energy needs rather than tissue synthesis, and hydrolysis of fat stores could lead to excessive production of ketones or by-products of fat metabolism. Pregnant women appear particularly susceptible to ketosis. Ketosis, as evidenced by studies in pregnant diabetic women, is poorly tolerated by the fetus and may impair fetal neurological development.

Table 24-2 outlines some characteristics of mothers who are at increased risk for delivering small-for-

Table 24-2. Increased Risk Characteristics

Mothers at Risk for Small-for-Gestational-Age Infants	*Families at Risk for Failure-to-Thrive Infants*
Below age 14	Single mothers
Over age 30	Parents under age 21
Underweight at the time of pregnancy	Welfare recipients
Inadequate weight gain	Non-breast-feeding mothers
Alcoholic mothers	Frequent change in household, location of residence, or relationships
Smoking mothers	Mother over age 30 who has four or more children and the last child is young
Mothers who have had multiple pregnancies delivering other low-birth-weight infants	

gestational-age infants and infants who exhibit failure to thrive.

There are greater risks of pregnancy complications at both ends of the age cycle in reproduction, specifically in the very young adolescent, 14 or younger, and in women over 30 years of age.[40] In general, the outcome of adolescent pregnancy is determined by the complex interaction of socioeconomic, health, psychological, and emotional factors. Support by the family, and the attending physician and staff is essential for a positive pregnancy outcome. Group classes with other pregnant teens can be beneficial in providing important information on pregnancy and infant care, as well as providing emotional support.

In order to provide some practical guidelines for the primary care physician when recommending diets for children, adolescents, and pregnant women, an expanded food selection guide, based on the basic four food groups, is presented in Table 24-3.[41]

The identification of nutritional risks and problems among pregnant women, children, and adolescents, as well as knowledge of appropriate medical and nutritional intervention, is important for the primary care physician. Detailed information concerning these health problems and related risk factors, as well as nutritional assessment and intervention guidelines, is provided in Appendices A and B.[41] Also, several federally sponsored food assistance programs are available at the community level for these target groups; Appendix C outlines these programs and their administrative agencies. Locally, the physician should check with state health and/or welfare departments for eligibility requirements and availability of these programs.

Unusual Dietary Practices and Consequences in Pregnancy

The primary care physician dealing with prenatal care needs to be aware of cultural, habitual, or religious practices of patients that can have an effect on the developing fetus.

The Committee on Nutrition of the Mother and Preschool Child of the Food and Nutrition Board, National Research Council, has issued a report on alternative dietary practices and nutritional abuses in pregnancy.[42] The premise of the report is that some groups of pregnant women and babies are at special risk because of eating and drinking practices that may deprive them of essential nutrients or expose them to toxic substances. Cultural and religious taboos may influence women to avoid foods that are needed during pregnancy. Excessive use of tobacco, alcohol, or other drugs may pose a hazard by interfering directly with fetal development and by reducing the mother's food intake and ability to utilize certain nutrients effectively.

The physician and staff, including dietitian and nurse, are advised to evaluate the patient's total diet; to establish an empathic, non-judgmental dialogue; and to encourage the use of foods that meet the nutritional needs of the women, whatever the foods may be. Many Americans do not eat the orthodox "middle class diet." For example, many Black, Asian, and Hispanic Americans do not drink milk or eat cheese; health care counselors need to recognize this difference and suggest alternative sources of calcium. Some specific areas of concern are identified below.[42]

Table 24-3. Food Guide for Balanced Diets

Food Group	Serving Size	Major Nutrient Contributions	Minimum Recommended Number of Servings		
			Child	Teenager	Pregnant Woman
Dairy Products					
milk	1 C	calcium, vitamin	3	4	4
cheese	1 C	D, protein,			
yogurt	1½ oz	phosphorus,			
cottage cheese	1 C	riboflavin			
Meat and Meat Alternates					
meat (beef, pork, etc.)	3 oz	protein, zinc, iron,	1½	2	3
fish	3 oz	thiamin,			
poultry	3 oz	riboflavin, niacin,			
dried beans	1 C	vitamin B_{12}, folic			
eggs	2	acid, vitamin B_6			
peanut butter	4 T				
peanuts, other nuts	3 oz				
Vitamin A Vegetables and Fruits					
broccoli	½ C	vitamin A,	½	1	1
carrots	½ C	magnesium,			
collards	½ C	vitamins C and			
green peppers	½ C	B_6, folic acid,			
spinach	½ C	fiber*			
sweet potato	½ C				
winter squash	½ C				
papaya	1 C				
cantaloupe	¼ melon				
plums	1 C				
apricots	3				
Vitamin C Fruits and Vegetables					
cantaloupe	¼ melon or 1 C	Vitamin C, carbohydrate,	½	1	1
oranges juice	1 or 6 oz	niacin, vitamin A,			
grapefruit juice	1 or 6 oz	folic acid, fiber*			
tomatoes juice	1 or 1 oz				
strawberries	½ C				
watermelon	½ C				
papaya	½ C				
broccoli	½ C				
raw cabbage	1 C				
green pepper	½ C				
brussels sprouts	½ C				
Other Fruits and Vegetables					
banana	1	carbohydrate,	2	2	2
apples juice	1 or 6 oz	vitamin B_6, folic			
pears	1	acid, niacin,			
grape juice	½ C 6 oz	potassium			
potatoes	1 sm or ½ C				
corn	½ C				
peas	½ C				
beets	½ C				
green beans	½ C				
Enriched or Whole Grain Breads and Cereals					
bread	1 slice	thiamin,	4	4	4
roll, biscuit, or muffin	1	riboflavin, niacin,			
crackers	4 small	carbohydrate,			
tortilla	1	protein, iron,			
ready-to-eat cereal	½ C	magnesium,			
pasta	¼ C	fiber*			
rice	¼ C				
Miscellaneous					
butter, margarine	1 t	linolenic acid,	Depends on caloric need		
oil	2 T	vitamin E,			
salad dressing	1 T	carbohydrate			
sour cream	1 T				
cream cheese	1 T				
mayonnaise	1 t				
gravy	2 T				

Adapted from King JC, Cohenour SH, Corrucini CG, Schneeman P. Evaluation and modification of the basic four food guide. *J Nutr Ed* 10:27, 1978.
*Fiber is not an essential nutrient but is an important dietary constituent.

From Brown, J.E.: "Nutrition Services for Pregnant Women, Infants, Children, and Adolescents." *Clinical Nutrition*, 3(3):100-108, 1984, p. 103. Used with permission of the publisher.

Tobacco

Cigarette smoking is one of the most preventable causes of low-birth-weight infants in the U.S.

Nicotine and carbon monoxide cause hypoxia to the body's tissues and place the fetus in a chronic state of hypoxia. Pregnancy complications, such as vaginal bleeding, are 25% greater among pregnant women who smoke less than one pack/day and 92% greater among women who smoke more than one pack daily as compared to non-smokers. Smoking is one of the most preventable causes of low-birth-weight infants in the U.S. On the average, infants born to heavy smokers are about 280 gm (about 0.6 lb) less at birth than infants of non-smokers. If the mother can be convinced to quit in the first trimester of pregnancy, the negative effect is more limited.

Caffeine

Animal studies have indicated possible birth defects from high levels of caffeine, but the findings have not been corroborated in humans. Therefore, the Committee recommended "moderation in caffeine intake during pregnancy."[42]

Over-the-Counter Drugs

The indiscriminate use of over-the-counter drugs during pregnancy is discouraged.

Since it is unethical to directly study the effects of numerous drugs on the pregnant woman, human research evidence is limited. Animal studies indicate that salicylate causes skeletal defects in rodent fetuses and that acetominophen can cause birth defects in animals. The Committee recommended that until more definitive data are available, indiscriminate use of over-the-counter drugs during pregnancy is to be discouraged.[42] Use of prescription drugs must be evaluated on a risk-benefit ratio and should be monitored carefully.

Vegetarian Diet

Vegetarians who drink milk and eat egg products generally maintain adequate nutrition during pregnancy, but vegetarians who avoid all animal products are at risk

of giving birth to abnormally small infants. The diet of strict vegetables is likely to be low in vitamin B_{12}, riboflavin, calcium, vitamin D, iron, and possibly zinc. Practitioners should prescribe high-energy, high-density foods to assure sufficient weight gain and successful lactation. Appropriate supplementation with at-risk nutrients such as B_{12} and calcium should reduce risks for deficiency.

Pica

This little understood practice of eating non-foods such as laundry starch, clay, or dirt is relatively prevalent among low income, rural Blacks in the South, although it exists in other regions and among other ethnic groups. Cases of toxemia, hypertension, and impacted bowels have been reported. If pica is excessive, other essential foods may be displaced in the diet; this could contribute to malnutrition. Some substances could contain toxic contaminants as well. The relationship between pica and iron deficiency anemia remains obscure.

The Fetal Alcohol Syndrome

About 1/3 of infants of mothers who drink heavily (more than 2 oz of alcohol/day) are growth-retarded. The damage done to the brain and neurological system of these infants is permanent, and throughout their lives victims of fetal alcohol syndrome remain two standard deviations below average for height and weight.

Infants of mothers who drink can develop a wide range of abnormalities, collectively referred to as the fetal alcohol syndrome (Table 24-4), as well as micro- and macro-nutrient deficiencies. About 1/3 of infants whose mothers are heavy drinkers (greater than 2 oz of ethanol per day) are growth-retarded, with a lower incidence (5-10%) of growth retardation in mild to moderate drinkers.

Research with animals indicates that alcohol interferes with organ development even when the nutritional status of the animal is maintained. It is not yet shown to what extent the defects of fetal alcohol syndrome are dependent on the amount of alcohol consumed, the genetic predisposition, and/or the nutritional status of the mother. However, it can be supposed that drinking alcohol in excess of the liver's ability to detoxify it results

Table 24-4 Major Features of Fetal Alcohol Syndrome Observed in 245 Advanced Cases

Feature	Manifestation	
	Present in more than 80% of patients	**Present in more than 50% of patients**
Brain Injury		
Intellectual	Clear mental retardation	
Neurological	Too small head (microcephaly)	Poor coordination (hypotonia)
Behavioral	Irritability in infancy	Hyperactivity in childhood
Growth Impairment		
Prenatal	Significant reduction in weight and height	
Postnatal	Significant reduction in weight and height	Disproportionately decreased fat stores
Facial Characteristics		
Head circumference	Too small	
Eyes	Short palpebral fissure	
Nose	Hypoplastic philtrum	Short upturned
Maxilla		Hypoplastic
Mouth	Thinned upper vermilion Retrognathia in infancy	Micrognathia or prognathia in adolescence

From Iber, F.L.: "Fetal Alcohol Syndrome." *Nutrition Today*, 15:4-15, 1980, p. 8. Used with permission of the publisher.

in alcohol reaching the fetus. There is some evidence from animal research that moderate alcohol ingestion by pregnant animals affects the learning ability of the offspring, and the defect can be correlated with the amount of alcohol consumed by the animals.[42] However, it is difficult to apply these data to humans. Further research is necessary to evaluate the effects of binge drinking at critical periods of brain growth versus the consistent daily consumption of ethanol.

What is known in fetal alcohol syndrome is that the damage done to the brain and neurological system is permanent. The circumference of the head is smaller than it should be; the facial and neurological impairments remain throughout life. Unlike infants who suffer from undernutrition, there is no catch-up growth or development.[43,44] Fetal alcohol syndrome victims remain more than two standard deviations below average for height and weight. A possible explanation for this is a direct insult of ethanol to cell proliferation resulting in decreased total number of cells.

Incidence of Fetal Alcohol Syndrome

The prevalence of fetal alcohol syndrome in the U.S. is not known. The disease was first identified in Seattle in 1973. Since then it has been estimated to include one out of every 900 live births. Extrapolated to the entire country, this could result in at least 12,000 children born each year with the anatomical and mental deformities of fetal alcohol syndrome. This could make it the most common birth defect of which we are currently aware.

Recommendations

What is the best answer the physician dealing in prenatal care can give the pregnant woman regarding a safe level of alcohol consumption?

There is no safe level of alcohol consumption for the pregnant woman, based on the availability of current research data.

The most conservative answer, and that which is recommended by the Committee on Nutrition of Mother and Pre-School Child, is that there is no safe level of alcohol consumption.[42] Therefore, any woman contemplating pregnancy should avoid all alcoholic beverages from the time of conception until the child is born. To avoid the striking structural changes of fetal alcohol syndrome, some experts recommend no more than four drinks per day. But this limit depends on a number of interrelated variables that make setting specific limits very difficult. The best advice remains, "No alcohol during pregnancy."

Alcoholic women, like alcoholic men, frequently abuse other toxic substances, in addition to alcohol, that can affect the fetus. This is especially true for teenagers and young adults. They take more drugs (such as tranquilizers), drink more coffee, and smoke more cigarettes than others. However, recent evidence lends strong support to the belief that alcohol itself is the primary factor in fetal alcohol syndrome.

Epidemiologic investigations of the use of caffeine, nicotine, tranquilizers (such as valium), and malnutrition fail to reveal physiological and anatomic patterns of fetal alcohol syndrome when alcohol is not abused.[43] Therefore, if the mother can be convinced to stop drinking during the course of her pregnancy, she should increase the chances of having a normal, healthy child.

Anorexia Nervosa

Starvation and malnutrition can be self-induced or be a result of society's failings. The former is the case in the eating disorder, anorexia nervosa. Although cases of anorexia nervosa have been reported throughout history (the earliest description of the disorder was published in 1689), it was considered a rare and bizarre disorder. Recently, however, reported cases of anorexia nervosa are on the rise, as is the body of research literature on the subject. Consequently, it is now possible to clinically describe and characterize the specific syndrome and to differentiate it from atypical or secondary anorexia.

Anorexia nervosa is primarily a disease of adolescent girls. Anorexics eat ritualistically, have distorted body images, and often exhibit hyperactive exercise patterns. The presence of amenorrhea, subnormal body weight, and denial are useful in the diagnosis of anorexia nervosa.

Anorexia nervosa is primarily a disease of adolescent girls, with a bimodel risk of onset at ages 14 and 18 years and a female-to-male incidence ratio of 9:1.[45] The leading dynamic issue of anorexia nervosa is the relentless pursuit of thinness and a fanatic fear of becoming fat.[46] Table 24-5 lists the common diagnostic criteria of the disorder. Since diagnostic uncertainty is common,

Table 24-5. Generally Accepted Criteria for Diagnosis of Anorexia Nervosa

A. Onset between the ages of 10 and 30 years

B. Weight loss of at least 20% of original body weight

C. A distorted attitude toward eating, food, or weight:
   1. Fear of fatness, especially associated with fear of loss of control of eating
   2. Desire to produce lower and lower body weight, especially associated with change in body image manifested by thin or cachectic patients considering themselves normal or overweight (perceptual distortion)
   3. Denial of illness and nutritional needs
   4. Preoccupation with thoughts of food and increased food-related activities
   5. Unusual behavior related to food: secretive disposal, hoarding, food fads, starvation, extreme limitation of calories, or self-induced vomiting

D. Amenorrhea (in females)

E. At least one of the following:
   1. Excessive physical activity
   2. Food binges
   3. Use of diuretics or laxatives to lower weight
   4. Bradycardia
   5. Lanugo hair

F. No known prior medical illness associated with significant weight loss

G. No known prior psychiatric illness of which serious weight loss is a regular symptom, especially:
   1. Primary depressive illness
   2. Obsessive-compulsive disorders
   3. Schizophrenia with delusions related to eating
   4. Stimulant medication abuse

From Anderson, A.E.: "Anorexia Nervosa," in *Manual of Clinical Nutrition*, Jackson, H.N., et al. (eds.). St. Louis, MO: C.V. Mosby Co., 1983, p. 26.2. Used with permission of the publisher.

care must be taken to be sensitive to more mild forms of the disorder as well as to distinguish it from eating disorders secondary to psychiatric conditions, such as depression, hysteria, schizophrenia, and obsessive-compulsive states.[45,46]

Epidemiology

The primary care physician should consider the possibility of anorexia nervosa in any young woman who diets below a reasonable weight. Early and accurate diagnosis can result in reduced morbidity and mortality, and earlier treatment leads to improved outcome.

Although anorexia nervosa has been described as a disorder affecting primarily white, middle-class girls, the primary care physician should be sensitive to the possibility of anorexia nervosa in any young woman who begins dieting and continues below a reasonable weight. This is especially important when there is a preoccupation with thoughts of food, fear of obesity, and perceptual distortion characterized by overestimation of body size. Early and accurate diagnosis can result in reduced morbidity and mortality, and early treatment leads to improved outcome.[47] Borderline anorexics may actually not have reached suboptimal body weight (below 25% of normal body weight), but because of excessive dieting they have lost a significant amount of body weight and have developed amenorrhea.

Although the syndrome is found most frequently in

women, it should be considered in young men with similar symptoms. In the last decade, men have increasingly shared with women the emphasis on slimness through exercise and dietary restriction. Athletes are particularly susceptible, and case studies of "obligatory runners" who control body weight and who achieve a large amount of their self esteem from intensive running have been described in the literature as male anorectics.[48]

The primary care physician should strongly discourage methods of weight control that over-restrict total energy intake and foster binge-purge behavior by the dieting individuals.

Many popular fad diets, such as some of the liquid and/or very-low-calorie weight-loss programs, may contribute to binge-purge eating behaviors. Over-restriction of calories (less than 1000 kcal/day) normally leads to increased desire for food, and consequently many dieters yield to a binge. This is followed by feelings of guilt, diminished self esteem, and purging, either through restricting food intake and/or self-induced vomiting, laxative abuse, or diuretic abuse. Such methods of weight control should be strongly discouraged by the physician. This also includes discouraging some of the popular weight-loss centers and clinics popping up throughout the nation. Any program that excessively restricts voluntary food intake sets up the participant for this type of behavior.

Certain subgroups of the population are more inclined to have anorexia nervosa members. These include dancers (specifically ballet dancers), models, gymnasts, runners, swimmers, and even wrestlers.

Psychological Profile

Some individuals appear to be predisposed to anorexic behavior. Typically the person is perfectionistic, self-critical, obsessive, and not psychologically insightful.[49] Some of these traits can be associated with the direct effects of starvation and parallel Keys' description of voluntary starvation in Minnesota volunteers.[50] When body weight is restored to more normal levels, the anorexia nervosa patient is better able to cope with and participate in the treatment process. Table 24-6 lists some of the more typical anorexia nervosa behavior patterns.[45] These represent behaviors isolated by research to date and are subject to further modification as more research is conducted.

Table 24-6 Typical Anorexic Behavior

1. Preoccupation with food (e.g., excessive thoughts of food, recipe collection, cooking for others)
2. Avoidance of eating in company
3. Periodic loss of control with eating binges
4. Self-induced vomiting
5. Laxative and/or diuretic abuse
6. Heavy consumption of low-calorie bulk foods (such as salads and carrots)
7. Layers of clothing for camouflage and insulation
8. Withdrawal from social relationships
9. Deceptive behaviors
10. Emotional lability, insomnia, loss of libido
11. Conceptual and perpetual errors, distorted self-image
12. Hyperactivity, excessive physical activity.

Adapted from McSherry, J.A.: "The Diagnostic Challenge of Anorexia Nervosa." *American Family Physician* 29(2):141-145, 1984.

The primary care physician may find these typical behavior patterns helpful in diagnosing anorexia nervosa.

Body Image Distortion

Anorexics typically overestimate their body size by as much as 20% to 80% and are not usually successful in overcoming the disorder until body image disturbances are resolved.

Garfinkel has indicated that patients with anorexia nervosa overestimate body size by 20-80%.[51] Patients recognize that medically they are thin, but perceptually they do not feel thin nor do they see themselves as thin. It is this perceptual distortion that drives weight lower and lower. Any treatment program needs to attempt to correct the perceptual disturbance through a variety of techniques.

Physiological and Nutritional Changes

Since denial is a feature of the disorder, patients with anorexia nervosa do not typically seek medical attention for their obvious problems. However, they may come to the physician or be brought by a parent because of

amenorrhea, weakness, fatigue, fainting spells, presence of lanugo hair, and numerous gastrointestinal complaints, such as diarrhea, constipation, abdominal pain, and bloating (Table 24-7).[45,49,52]

Table 24-7. Common Complaints in Anorexia Nervosa

Amenorrhea, oligomenorrhea
Fainting spells
Fatigue
Feelings of coldness
Abdominal bloating, distention, cramping
Reduced libido
Insomnia
Constipation

Most of these symptoms can be attributed to the effects of starvation itself, and there is some question as to whether there are specific physiological changes unique to anorexia nervosa. For a woman of average height, the starvation symptoms become especially prominent at a weight less than 90 pounds. Also, if patients use unnatural methods for weight loss, such as laxatives, diuretics, or self-induced vomiting, they may manifest hypokalemia, alkalosis, electrolyte disturbances, heart arrhythmias (sometimes fatal), esophagitis, and enamel demineralization.[45,52] Maturational development in starvation can be halted and if nutritional and psychiatric therapy are not initiated immediately, especially in the young adolescent, permanent effects on reproductive physiology and growth and development can result.

Treatment

The primary care physician can play an important role in the treatment of anorexia nervosa. By identifying the disorder for the patient and the family and directing them to an appropriate treatment program, while providing medical care and psychological support, the physician can be the pivot of the treatment program.

The primary care physician can play an important role in the treatment of anorexia nervosa. If a patient is suspected of having an eating disorder, either by the family or the physician, immediate and aggressive treatment is indicated. Often a frantic and worried parent will be the first to contact the physician. A compassionate and reassuring approach by the physician is recommended. Although there are certain family characteristics more common in the family of an anorectic, such as overprotectiveness, rigidity, parental conflict, and alcohol and drug abuse, these are by no means universal. Many families are confused and frustrated with their anorexic family member and ridden with guilt. Helping families receive the support they need is the role of the physician.

Nutritional rehabilitation and psychological counseling are the cornerstones of treatment, which include family therapy and support groups. It is now recognized that since many of the symptoms of severe anorexia nervosa are the result of starvation, meaningful psychotherapy is not productive until body weight is restored above a critical level.[52]

Treatment can occur on an outpatient or inpatient basis. The decision to hospitalize the patient with anorexia nervosa depends upon (1) the severity of weight loss (below 25% of ideal body weight); (2) the lack of success of outpatient therapy; (3) the presence of metabolic abnormalities, such as hypokalemia, alkalosis, severe depression, or suicidal ideation; and (4) the ability of the family to cope with the patient's problems. There are numerous inpatient treatment programs and philosophies, but the most successful tend to involve the team approach, including the physician, psychologist, nutritionist, nursing staff, and social worker. Table 24-8 lists some suggested goals of treatment for anorexia nervosa.

The recommended sequence for the treatment of anorexia nervosa consists of nutritional rehabilitation, psychotherapy, maintenance, and follow-up.

The recommended sequence of treatment for both inpatient and outpatient programs consists of:

1. *Nutritional Rehabilitation.* A gradual increase in the caloric intake is recommended, not to exceed 200 to 300 kcal at a time. Weight stabilization is the first

Table 24-8. Goals of Treatment for Anorexia Nervosa

1. Normal weight (25-50th percentile for height ± 3 lb)
2. Normal eating behavior
3. Psychological social maturity, including:
   a. understanding own temperament,
   b. willingness to accept maturation and to take responsibility for own behaviors,
   c. social skills appropriate to age, and
   d. assertive skills
4. No preoccupation with food or weight issues
5. Normal menses if female; normal sexual drive in males and females
6. Return to work or school with effective functioning
7. Satisfactory working relationships
8. Adequate self-esteem

From Anderson, A.E.: "Anorexia Nervosa," in *Manual of Clinical Nutrition*, Jackson, H.N., et al. (eds.). St. Louis, MO: C.V. Mosby, 1983, p.26.13. Used with permission of the publisher.

goal, followed by very gradual weight gain so that the patient can emotionally accept an increased body weight and avoid gastrointestinal complaints. A 1400 to 1600 kcal, low-fat, lactose-free, low-simple-sugar diet may be tried initially. Behavior modification programs have been described that have been successful in initiating the eating process.[49] Only in rare and extreme circumstances is forced feeding via tube or hyperalimentation necessary.

2. *Psychotherapy.* Psychotherapy is individualized to the patient. The most common concerns of the anorexia nervosa patient are fear of loss of control, an inner sense of lack of effectiveness, lack of individualization from the family, and fear of sexual development.[52] A major aspect of therapy involves helping the patient to identify inner emotional states and to deal directly with them rather than indirectly through the use of food. Emphasis on improving self esteem, improved feelings of worthiness, and improved body image are important. Multidimensional approaches are the trend in treatment, including group, individual, and family treatment. Table 24-8 outlines the goals of treatment for anorexia nervosa.
3. *Maintenance Period and Follow-up.* Once the patient has returned to more normal body weight and accomplished what is possible in individual, group, and family counseling, the responsibility for choosing food and exercise should be gradually returned to the patient with encouragement and guidance. It is helpful to choose a weight range rather than a weight goal so the patient can negotiate within three pounds; most patients will not accept weight approximating the 50th percentile for their age or height because it is felt to be excessive.

A small number of patients appear to recover from anorexia completely. A larger proportion, perhaps 50%, improve substantially but regress in times of stress; about 25 to 30% remain chronically ill with frequent hospitalizations. There is an estimated 10% mortality rate from this disorder. Often, eating remains a difficult chore for patients even after treatment, but with practice and the development of a more healthy personality, their general eating behaviors become more appropriate. The younger the patient and the earlier the disorder is treated, the greater the likelihood for complete recovery.

Prevention

There may not be specific means to prevent anorexia nervosa, but the recent increase in research and the widespread dissemination of information about the signs and symptoms of the disorder have done much to increase public awareness. With increased public awareness, families and affected individuals tend to seek earlier treatment. Parents, teachers, physicians, and others should be responsive to teenage girls and boys who appear preoccupied with food and body weight and who resort to excessive dieting and/or exercise to reduce body weight below reasonable levels. The emphasis in western

societies on extreme slimness may be a contributory cause to the increase in incidence of anorexia nervosa, but it will take years to change this value. Support groups and national organizations are developing across the nation to provide public education, prevention, and treatment programs for individuals with eating disorders. Appendix D lists some of these groups from which further information can be obtained. Appendix E outlines some national centers which specialize in the treatment of eating disorders. Also, many large medical centers are developing inpatient and outpatient programs on a local basis.

Bulimia

Bulimia can be characterized by a powerful and intractable urge to eat, self-induced vomiting to rid the body of eaten foods, and a marked fear of becoming fat.

Another eating disorder that has been receiving attention recently and appears to affect a great number of individuals is bulimia or bulimia nervosa. The Latin derivative of the word is "insatiable appetite," the Greek derivative is "ox hunger," but bulimia is best known as the binge-purge syndrome. Russell has identified three characteristics of bulimia.[53] These are: (1) a powerful and intractable urge to eat, (2) the reaction to overcome the effect of overeating by self-induced vomiting and/or purgative abuse, and (3) a marked fear of becoming fat. Although some patients with anorexia nervosa exhibit bulimic behavior, it is now recognized that bulimia is a separate eating disorder with its own clinical features. Table 24-9 lists the similarities and distinguishing features between anorexia nervosa and bulimia.[54] Both groups have excessive concern (preoccupation) with food and weight control. They both rely on excessive measures for weight control, including vomiting, laxative use, diuretic abuse, and dieting. In addition, both are usually perfectionistic and have unrealistically high expectations for themselves.

Bulimia is difficult to diagnose because of the nature of the disorder and the lack of overt physical symptoms in the early stages.

Bulimia is commonly found among young women age 18 and older. Five to ten percent of college women are estimated to have bulimia. The victims are primarily from middle and upper socioeconomic classes, and most have some college education. More than half are close to their proper weight. This is one reason the disorder is more difficult to diagnose. Subjects do not appear obviously ill to the physician. Also they are ashamed of their behavior, which they refer to as "disgusting," and are not likely to discuss it with others. Bulimics have been known to hide the behavior for years from family,

Table 24-9. Similarities and Distinguishing Features of Anorexia Nervosa and Bulimia

Anorexia Nervosa	Bulimia
often denies problem (may be proud of weight loss)	recognizes abnormal eating pattern
exhibits significant weight loss	usually within 10 to 15 pounds of normal body weight
usually maintains rigid control of eating	often feels loss of control of eating
introverted	extroverted
turns away from food to cope	turns to food to cope
has difficulty in accurately assessing body size	may be better able to assess body size but still has body image distortion

From *National Anorexic Aid Society (NAAS): Newsletter,* National Anorectic Aid Society, Inc., Westerville, Ohio, January-March (Volume 2, Number 2, 1984). Used with permission of the National Anorectic Aid Society.

spouses, and friends. However, they can come to a point where they are totally out of control and where binge/purge episodes can reach as many as 20 or more per day.

Self-induced vomiting is the most common method of purging, initiated immediately following eating. Other methods of purging include laxative abuse; amphetamine, caffeine, and diuretic use; excessive exercise; and fasting.[53-55] This behavior is not without its medical risks. Vomiting can be gag-initiated or via emetics, such as syrup of ipecac or emetine which are cardiotoxic and can be overdosed. Repeated vomiting can lead to a very specific type of dental disease featuring perimylolysis, absence of stain, temperature sensitivity, and amalgam "islands." The family dentist may be the first health professional to actually recognize the possibility of bulimia.[56] Other side effects of bulimia are listed in Table 24-10.

Psychopathology

Psychologically, bulimic patients are often described as having high standards coupled with low self-esteem. They are often achievement-oriented, obsessive, and perfectionistic. Socially they can be extroverted, but as the disorder progresses, they resort to periods of moodiness and irritability. Next to the preoccupation with food and body weight, Russell found that depression was the most prominent feature of the patients' mental states.[53]

Treatment and Prognosis

The primary care physician should be sensitive to the possibility of the binge-purge syndrome in any patient, particularly the young female who is dieting and is excessively concerned about body weight.

Again, the role of the primary care physician in dealing with this eating disorder is one of recognition, treatment, referral, and support. The diagnostic difficulty with bulimia is the lack of apparent symptoms until the disorder is very severe and of long-term duration. At this point, treatment becomes considerably more difficult. Actually, the physician should be sensitive to the possibility of binge-purge syndromes or behavior patterns in any female patient who is "dieting" or is excessively concerned about her body weight. Appendix F provides a questionnaire used by Halmi, et al., to evaluate binge-eating and vomiting in a college population.[57] This questionnaire can be used in your practice, or you can personally ask a few key questions which may isolate the behavior.

It is recommended that the physician investigate the credentials and background of any eating disorder treatment program, facility, or in-

Table 24-10 Possible Medical Complications of Commonly Used Weight-Regulation, Weight-Loss Methods

Vomiting	Diuretic Abuse	Laxative Abuse
• Parotid gland enlargement (neck area) • Erosion of tooth enamel and increased cavities • Tears in esophagus • Chronic esophagitis • Chronic sore throats • Difficulty swallowing • Stomach cramps • Digestive problems • Anemia • Electrolyte imbalance	• Hypokalemia (low potassium): fatigue; diminished reflexes; if severe, possible cardiac arrhythmia; if chronic, serious kidney damage • Fluid loss: dehydration, lightheadedness, thirst	• Non-specific abdominal complaints (cramping, constipation) • Sluggish bowel functioning ("cathartic colon") • Malabsorption of fat, protein, and calcium

Combinations of these methods can dangerously affect potassium regulation and fluid balance.

dividual practitioner before referring a patient to ensure that qualified professionals are providing the treatment.

There are several modes for treatment of bulimia, depending on the location of the patient. Hospitalization may be required, preferably at a medical center which specializes in treating eating disorders. University student mental health clinics are increasingly adding the treatment of eating disorders to their programs because of the increasing number of cases on college campuses. Registered dietitians in private practice are health professionals who have considerable experience with treating eating disorders and, along with a clinical psychologist who specializes in eating disorders, can implement an effective treatment program. Communities often will have eating disorder societies or support groups, such as the National Anorexic Aid Society, Inc., to which the patient can be referred (Appendix D). The physician should investigate the credentials and background of any treatment program, facility, or individual practitioner before referral to ensure that qualified professionals are providing the treatment.

If the patient appears resistant to treatment, the physician should not give up but rather should solicit the help of family and friends if possible. Patient confidentiality is important to maintain; but if it appears that a legitimate health risk is imminent, then treatment becomes essential.

The treatment of bulimia is still in the developmental stages and reports of successes and failures are abundant. It appears that dietary restrictions should be minimal in any treatment approach.[53] Treatment emphasizing self-acceptance and more effective coping skills seems necessary, in which patients are encouraged to abandon the self-destructive concept of self worth as defined by body weight. Modification of body weight and body image attitudes is also important in discussions of healthy body weight versus society's excessive emulation of extreme thinness. Cognitive restructuring, combined with behavioral techniques to avoid overrestraint and binging, has been beneficial in controlling the behavior. Admission to a hospital or in-patient program is essential if the possibility of suicide is high or complications of vomiting (hypokalemia) or laxative abuse are severe.

Long-term follow-up studies on the treatment outcome of bulimia are not yet available, though short-term data are available. Preliminary observations indicate prognoses less favorable than in true anorexia nervosa, probably because bulimia is more resistant to treatment. Therapists have not had extensive experience at this time in treating the disorder. Physical complications of bulimia are more frequent and dangerous, and the risk of suicide is greater than in anorexia nervosa.[53]

The Role of Nutrition in the Premenstrual Syndrome

Premenstrual syndrome (PMS) is loosely characterized by a cluster of physical and psychological symptoms that are temporarily limited to the week or so preceding menstruation and relieved by the onset of menses. To date no hard evidence has linked an endocrine abnormality to PMS. Improvement of PMS symptoms in many studies can be attributed to placebo effects and not the treatment *per se*.

The dramatic change in mood, behavior, cognition, and somatic functioning in some women in relation to their menstrual cycle has been the focus of considerable media attention recently. Several popular books have been published and specialty clinics have emerged which are designed to treat women suffering from a variety of menstrually related symptoms.

Unfortunately, despite 50 years of study, relatively little is known about the relationship of menstruational disorders to mood and even less is known about how diet interacts with these factors.[58] Although there is a widespread lack of concurrence on the definition of this disorder, Dr. Katherine Dalton, a British physician, has labeled it premenstrual syndrome (PMS). PMS is loosely characterized by a cluster of physical and psychological symptoms that are temporarily limited to the week or so preceding menstruation and relieved by the onset of menses.[59] Table 24-11 lists some commonly reported symptoms of PMS.[58]

Dalton reports the almost entirely unsupported theory that PMS is, in all cases, a hormonally based disorder resulting from a relative deficiency of progesterone during the latter part of the luteal phase and that the effects of this endocrine imbalance can be alleviated by

Table 24-11 Some Symptoms of Premenstrual Syndrome

Altered Emotional State	Tension, anxiety, depression, irritability, hostility
Behavioral Changes	Avoidance of social contact, change in work habits, tendency to pick fights, crying spells, increased or decreased libido
Somatic Complaints	Abdominal bloating, backache, headache, breast swelling or tenderness
Altered Appetite	Food craving or avoidance of certain foods
Motor Effects	Changes in coordination, clumsiness

Note: Many additional symptoms have been reported in the literature.

From Rose, R.M., and Abplanalp, J.M.: "Premenstrual Syndrome." *Hospital Practice*, 18(6):130, 1983. Used with permission of the publisher.

natural progesterone therapy.[60,61] Dr. Dalton testified at two murder trials in Great Britain and argued that the accused were suffering from severe PMS symptoms that led them to uncontrollable acts of aggression. The accused received a reduced or probated sentence, and this triggered a landslide of controversy.

At this time very little is understood about the pathogenesis of PMS. In recent years the probable etiologic role of an undefined endocrine imbalance has been stressed. Progesterone deficiency, hyperprolactinemia, estrogen excess, and an imbalance of the estrogen/progesterone ratio have been suggested. To date, no hard evidence linking a specific endocrine abnormality to premenstrual symptoms has been established.[59]

What is PMS? What is the incidence of this disorder in the female population? How can the primary care physician evaluate the research to date in this area? These are some difficult questions to answer. The list of references in this module provides several excellent reviews and criticisms of the research in this area. In general, the results of clinical trials so far have been erratic, with causal factors of PMS not clearly indicated through treatment regimens. Improvement is found in most uncontrolled studies, primarily due to placebo effects rather than the treatment *per se*. Other problems with the research include (a) lack of uniform criteria in defining PMS symptoms and their improvement; (b) inadequate methods for assessing symptoms, particularly when using retrospective assessment as compared to daily monitoring of symptoms including a baseline period; and (c) difficulties in measuring the severity of these symptoms.[60]

Several researchers have observed erratic eating patterns and poor dietary habits in women with PMS. Pyridoxine (40 to 100 mg/day) may be beneficial in some women with PMS, but further research is required. Otherwise women with definite PMS symptomatology can be encouraged to develop good health habits, including eating a balanced diet from a variety of foods. Nutritional counseling can be very beneficial and specific guidelines should be tailored to the individual patient's needs. Methods of weight control and behavior modification techniques to help control food cravings or binge eating are useful components of PMS counseling.

Research is limited regarding the role of nutritional factors in the etiology and treatment of PMS. Most of the nutritional modifications for PMS have been promoted by Dr. Guy E. Abraham of California who is now involved in the company OPTIMAL, Inc., which provides guidelines for setting up PMT (pre-menstrual tension) clinics and in selling a nutritional supplement, Optivite, for use by women with PMS.

Dr. Abraham makes certain unsubstantiated nutritional claims in the literature and in his booklet, "Premenstrual Blues."[62] His unsubstantiated nutritional claims include the following:

1. PMS symptoms can be alleviated by megadoses of pyridoxine (vitamin B_6) in doses ranging from 200 to 800 mg/day (RDA = 2-2.5 mg/day). Abraham claims many PMS women have a functional vitamin B_6 deficiency and that vitamin B_6 will reduce estrogen levels, increase progesterone levels,

and improve symptoms in PMS patients.[63,64]

2. Women with PMS have a chronic magnesium deficiency due to a diet high in refined sugar and dairy products. Calcium interferes with magnesium absorption, and sugar increases urinary excretion of magnesium.[64,65]
3. Symptoms of PMS are due also to increased extracellular fluid from sodium and water retention. It is suggested that there is a relative deficiency of dopamine which decreases the kidney's ability to excrete sodium. Vitamin B_6 deficiency is also implicated in the depressed dopamine levels.[64,66]
4. Women with PMS crave sweets, especially chocolate, and eat more food during the premenstruation phase than during other phases of the menstrual cycle. Such women have flat glucose tolerance curves and low levels of magnesium in red blood cells.[64,67]
5. A deficiency of prostaglandin, PGE, may be involved in the symptoms of PMS or PMT. Magnesium, pyridoxine (vitamin B_6), and cis-linoleic acid are required for PGE synthesis. Arachidonic acid is an antagonist to PGE production, and animal fats are high in arachidonic acid. Vegetable oils are high in linoleic acid. Therefore, it is proposed that a diet lower in animal fat and high in vegetable fats may help in PMS.[62]

In addition Dr. Abraham recommends vitamin E supplementation (300 IU/day) to improve the symptoms of breast tenderness often described by PMS sufferers.

Table 24-12 lists the dietary guidelines suggested by Abraham, some of which are derived from the above theories.[62] None of the above guidelines, other than vitamin B_6 and vitamin E supplementation, have been studied in well-controlled, double-blind studies to evaluate their effectiveness.

In two double-blind, placebo-controlled, cross-over studies, Stokes and Mendels found pyridoxine to be no more effective than placebo.[68] Abraham and Hargrove reported pyridoxine to be superior to placebo in reducing scores on a luteal-phase menstrual symptom questionnaire in 21 of 25 patients.[69] While Abraham and Hargrove used reasonable entry criteria, the absence of control cycle symptom scores prevents assessment of the placebo response.[69]

A double-blind, controlled study tested the use of vitamin E supplementation as treatment for PMS subtypes classified by Abraham. Improvement of PMS symptoms occurred and side effects of vitamin E supplementation were not observed. The authors suggest that the optimal dose of vitamin E is 300 IU/day (RDA = 30 IU/day).[70] All women in this study had benign breast disease; therefore, results may only be applicable to this sub-group. Verification of this study has not been published in the literature, and the effects of long-term vitamin E supplementation have not been studied.

Other concerns regarding the nutritional guidelines for PMS as recommended by Abraham include:

1. Use of strict sodium restriction by premenstrual women may counteract an unrecognized, adaptive mechanism of luteal water retention. The use of diuretics may aggravate PMS by promoting absolute or relative deficiencies of other ions, such as potassium and magnesium.
2. Use of vitamin B_6 supplementation looks promis-

Table 24-12 Dietary Guidelines for Premenstrual Tension

Limit consumpton of refined sugar (5 tsp/day), salt (3 gm sodium/day), red meat (3 oz/day), alcohol (1 oz/day), coffee, tea, and chocolate
Limit tobacco use
Limit intake of protein to 1 gm/kg body weight/day
Limit intake of dairy products to 2 servings/day.
Limit intake of fats, mainly saturated and cooked fats (less than 20% of total calories)
Increase intake of complex carbohydrates (60 to 70% of calories)
Increase intake of green leafy vegetables, legumes, whole grains, and cereals
Increase intake of cis-linoleic-acid-containing foods (safflower oil is an excellent source)
Rely more on fish, poultry, whole grains, and legumes as a source of protein and less on red meat and dairy products

From Abraham, G.E.: *Premenstrual Blues.* Optimax Corp., Rolling Hills Estates, CA, 1982. Used with permission of Optimax Corp.

ing; however, the appropriate dosage has yet to be determined, and the possibility of long-term toxic side-effects has not been ruled out.

3. Avoidance of foods which satisfy carbohydrate cravings may be counterproductive. Insulin response to carbohydrate intake increases the amount of tryptophan available for serotonin synthesis. Serotonin is thought to be a natural, self-administered anti-depressant by some researchers.
4. Magnesium replacement therapy should only be used when magnesium deficiency is documented. There is not enough evidence to recommend a dosage at this time. The possibility of long-term toxic side effects has not been ruled out.
5. A double-blind study showed that mefenamic acid, a prostaglandin inhibitor, is an effective PMS treatment.[71] Certain symptoms might be helped by this agent.
6. Some have attributed PMS to a deficiency of vitamin A, but none of the proposed mechanisms has been sustantiated; also, self-medication with vitamin A is potentially dangerous (see Module 23, Vitamins and Trace Minerals).

Until additional research is available, it will not be known if diet has a preventive role in PMS. The physician must explain this to patients since the lay press has published misleading diet recommendations which are premature conclusions based on limited research.

The approach recommended to the primary care physician in providing nutritional advice to the woman with definite symptoms of premenstrual syndrome is to evaluate her present lifestyle and eating patterns. Self-evaluation charts can be effective tools for evaluating symptom and mood swings. If she appears to have definite food cravings, erratic eating patterns, or abuses caffeine or alcohol, appropriate dietary recommendations can be made and may prove beneficial. Encouraging the patient to develop good health habits, such as sufficient sleep, three balanced meals per day, limiting the intake of salt, alcohol, caffeine, and tobacco, and participating in a daily exercise program, can go a long way in relieving some of the somatic complaints associated with PMS.

The Attention Deficit Disorder: Does Diet Play a Role?

The primary care physician should be cautious in the diagnosis of attention deficit disorder by utilizing the criteria established by the American Psychiatric Association and by avoiding unnecessary labeling whenever possible.

A fairly common problem in the pediatric population of the primary care physician is the hyperactive child. Parents and teachers are often frustrated in their attempts to control the behavior of these children and turn to the physician for help and guidance. The physician must first be aware of the many pitfalls in the diagnosis of this disorder. Currently, the acceptable diagnostic category for the symptoms used to describe hyperkinetic behavior is attention deficit disorder, with or without hyperactivity.[72] The most essential feature of attention deficit disorder is developmentally inappropriate inattention.[73]

In 1973, Dr. Benjamin Feingold suggested that the elimination from the diet of salicylates, artificial colors, and artificial flavors improved the behavior of 30 to 50% of hyperactive children in his practice.[74] He developed a diet protocol similar to the one in Table 24-13 (adapted from Conners, et al.), in which all naturally occurring and added salicylates, artificial colors, and artificial flavors are eliminated from the diet.[75] Several versions of the Feingold diet have been utilized to test hyperactivity, however none is consistent in format. This is due to the lack of evidence as to the specific "offending" chemical, if any, and the global nature of the Feingold diet.

The fundamental problem with Feingold's hyperactivity theory is that it is based on a model of behavior that completely ignores the "institutional" context within which "hyperactivity" or attention deficit disorder is generated and labeled. Hyperactivity is a form of deviance; i.e., a label for a particular set of child behaviors that do not conform to adult expectations and wishes. Scattered attention, aggressiveness, and authority problems are frowned upon by school teachers and

Table 24-13 The Feingold Diet or Kaiser-Permanente Diet

Type of Food	*Foods Allowed*	*Foods Omitted*
Milk, dairy products	Milk, white cheese, cottage cheese, plain yogurt or yogurt with no artificial color or preservatives	Prepared chocolate milk, all quick mix powdered drinks, all instant breakfast drinks, yogurt or cottage cheese containing artificial color, flavor, preservatives, or omitted fruits; yellow (colored) cheeses
Meat, poultry, fish, eggs	All fresh meats and eggs	Bologna, salami, other luncheon meats, frankfurters, sausages, meat loaf, ham, bacon, or pork (unless label specifies no artificial color, flavor, preservatives); all barbequed meats, stuffed poultry, self-basting turkeys, frozen fish fillets, dyed or flavored
Vegetables	All except those omitted	Tomatoes and all tomato products, cucumbers (pickles), vegetable mixtures with artificial color or flavor
Potatoes and substitutes	All fresh potatoes and potato chips (without preservatives, artificial colors, or flavors), all dried peas, beans, peanuts, peanut butter (without preservatives, artificial color, or flavor)	Barbecue potato chips, potato chips or peanut butter containing artificial ingredients
Fruit	Lime, lemon, pineapple, grapefruit, pear, bananas, juices, and nectars of the above	Apples, apricots, berries—blackberries, gooseberries, raspberries, strawberries; cherries, grapes, currants, raisins (and any products such as wine, wine vinegar, jellies, etc.); nectarines, oranges, peaches, plums, prunes, any juices of the above, apple ciders
Cereals and breads	Any bread or cereal without artificial colors or flavors; all flours	All breads and cereals with artificial colors and flavors; egg bread
Fats	Sweet butter (not colored or flavored), all cooking oils, and fats	Oleomargarine, colored butter
Soups	Any made with allowed ingredients and without preservatives, artificial color, or flavors	Most canned soups, soups made with omitted foods

Table 24-13 The Feingold Diet or Kaiser-Permanente Diet (Continued)

Desserts	Any product without artificial color or flavor; homemade ice cream (no artificial color or flavorings); gelatins, homemade or from pure gelatins with any permitted natural fruit or juices, tapioca, homemade custard, and puddings	All manufactured cakes, cookies, pasteries, sweet rolls, etc., pie crusts, frozen baked goods; many types of baking mixes; manufactured ice cream, sherbet, ices, gelatins, puddings, junkets
Beverages	Seven-Up, allowed fruit juices	Teas, all kinds; wine, beer, diet drinks, soft drinks, cider, omitted fruit juices
Sweets	Sugar, honey, homemade chocolate syrup, jellies or jams from permitted fruits, homemade candies	Commercial chocolate syrup, all manufactured candies (hard or soft)
Miscellaneous	Homemade mustard and mayonnaise, distilled white vinegar	Manufactured mustard, cloves, all mint flavorings and mint flavored or colored; cider, wine vinegar, catsup, chili sauce, almonds, almond flavoring or extract
Other non-food items	Neutrogena soap or salt and soda mixture for cleaning teeth	Aspirin, Bufferin, Excedrin, Alka-Seltzer, Emperin, Anacin, and other over-the-counter medications containing salicylates, artificial color, or flavorings; all toothpastes and mouthwashes, all coughdrops, all throat lozenges, antacid tablets, perfumes

Adapted from Conners, C.K., et al.: "Food Additives and Hyperkinesis: A Controlled Double-Blind Experiment." *Pediatrics*, 58: 154-166, 1976, p. 165.

parents since they pose problems of order and control. Labeling a child as hyperactive can be a way for parents or school officials to shift the burden of responsibility to a vaguely defined, scientific-sounding malady. This has been termed the "deviance-as-disease" model. The child's behavior is blamed on diet. Parents, teachers, and others then have the concrete, though difficult, problem to tackle of eliminating those harmful substances from the diet that cause the child's behavior. Therefore, the primary care physician needs to be aware of the problems inherent in such labeling and approach the diagnosis of attention deficit disorder from a very conservative orientation.

The Feingold hypothesis for hyperactive behavior is not based on well-controlled experiments of studying the effects of a diet free of artificial colors and flavors on specific well-defined behaviors. It is based on open trial observations in his clinical practice that can easily be attributed to placebo effect.

Problems with appropriate diagnosis of attention deficit disorder and objective, accurate, and reproducible methods of measuring these behaviors have made the research in this area difficult to evaluate. Feingold's claims have not been based on carefully controlled, double-blind experiments reproduced by a variety of researchers, but on his clinical observations of the improvement of subjective symptoms. Obviously the most frequent criticism of his research is that the changes

observed in the children on the diet could easily have been brought about by the increased interest and attention given the child by the family, teachers, physician, and others. The diet is a difficult one to follow and requires the cooperation of the family and others involved in feeding the child. Alteration in the family dynamics may be the cause of improvements in the child's behavior rather than the elimination of specific foods.

Other problems with Feingold's hypothesis include:

1. What is the mechanism of supposed toxicity to artificial flavors and colors; is it an allergic reaction or is it a toxic reaction to substances of low molecular weight?
2. How is hyperkinesis defined, and what specific behaviors are affected by the diet?
3. Which food substances, artificial colors, flavors, or salicylates are the most likely toxic agent or agents?[76]

Since his original publication, Dr. Feingold has modified his hypothesis to allow foods containing salicylates because most foods do not contain measurable amounts of salicylates. He now believes they are not the usual source of difficulty.

Several studies have been conducted so far to test the Feingold hypothesis. Connors has conducted several investigations, one of which showed brief decreases in attention spans in children receiving additive-containing foods that were not seen when the challenge diet was additive free. When behavior was rated by parents and teachers, no behavior differences were noted between the food additive period and the non-food additive period.[75,77]

Connors has since written a book entitled, *Food Additives and Hyperactive Children,* which has been criticized for inadequate testing of the Feingold hypothesis and arrival at conclusions regarding the effects of food colors and flavors on child behavior based on very inconclusive evidence.[78]

Other investigations of the effect of diet on attention deficit disorder have elicited some transient effects of challenge foods in these children one to two hours after ingestion, but have not exhibited any global changes or improvement in behavior or learning on a diet free of artificial colors or flavors.

Other investigations on the effects of diet on attention deficit disorder have elicited some transient effects of foods high in artificial colors and flavors one hour after ingestion by hyperactive children. However, researchers have not been able to identify any global changes or improvement in behavior and/or learning as rated by teachers or parents when hyperactive children were fed a diet free of artificial food colors or flavors.[75,79]

Further studies on these possible transient effects on behavior in attention deficit disorder children and better control of placebo effect by utilizing a true double-blind design are needed. In the meantime, the physician is faced with the challenge of helping the child with attention deficit disorder and his family by providing the best treatment program available. Several stimulant medications have proven very useful in improving symptoms in these children and, if used judiciously, can help the child get through difficult periods.[79,80] A review of medications prescribed for hyperactivity is provided in the references.[81] Drug therapy is considered only a part of the total program; physicians, parents, teachers, and support personnel must work together using behavioral management, educational evaluation, and remediation of academic problems.[81]

As for nutritional recommendations, a careful review of the child's diet is necessary to ensure receipt of sufficient nutrients and food energy to promote optimal growth and development. Listening to parent and child concerns, providing sound nutritional advice, and suggesting a multidimensional drug and behavioral program will be very useful in helping the attention-deficit-disorder child. Based on research to date, the modified Feingold diet cannot be recommended except in extreme cases when all other approaches have not provided positive results or when the parents refuse a medication trial. Harper, et al., found that the nutritional intake of children on the modified Feingold diet (which allows salicylate-containing foods) remained essentially unchanged from their normal diets and compared favorably with the Recommended Dietary Allowances.[82] Therefore, the diet is nutritionally adequate when foods with salicylates are included and does not pose a threat to overall nutritional status.

Hypoglycemia: Types, Diagnosis, Treatment, and Effect on Human Behavior

Reactive hypoglycemia has become a frequent diagnostic label in the past 10 years. It is promoted by the media as the cause of numerous physical complaints and is linked to any number of behavioral disorders, including alcoholism, drug dependency, and even anti-social and criminal behavior. Despite this trend, when available diagnostic criteria are strictly applied, idiopathic, postprandial hypoglycemia in the absence of alimentary tract surgery or diabetes is a very rare condition.

Scenario:

The patient comes to the physician complaining of a variety of symptoms, including tiredness, weakness, hunger, anxiety, headaches, and insomnia. She states that if she misses a meal or eats later than usual she has "attacks" of sweating, increased heart beat, nervousness (her hands shake), and faintness. She usually feels better about 20 minutes after eating. She has read about such symptoms in a recent article in *Glamour Magazine* which referred to the disorder as "reactive hypoglycemia." She wants to know if this is what is causing her symptoms and, if so, what should she do to feel better.

This is not an uncommon occurrence in a typical practice. Hypoglycemia has become a frequent diagnostic label in the past 10 years, applied often without any logical justification. Anecdotal data on hypoglycemia have been promoted by a host of popular books and magazine articles.[83,84] Also any number of behavioral patterns have been blamed on this disorder, including alcoholism, drug dependency, juvenile delinquency, poor concentration, poor academic performance, and anti-social, aggressive, and even criminal behavior such as murder and arson.[85-90] The seriousness of this trend is particularly disturbing from the social and moral standpoint of transferring responsibility for human behavior to a clinical disease over which the victim has no control. It also poses the medical dilemma of attributing a diagnosis to a set of symptoms and complaints when strict criteria for such a diagnosis have not been fully established. Furthermore, research evidence available to date indicates that when applying available criteria, idiopathic, postprandial hypoglycemia, in the absence of alimentary tract surgery or disorders or diabetes, is a very rare condition.

The purposes of this section are to

1. outline the problems in the diagnosis of postprandial hypoglycemia and distinguish it from other forms of hypoglycemia;
2. define a set of criteria for the diagnosis of the disorder based on available research evidence; and
3. provide a practical guide for the physician for the treatment of this disorder following diagnosis emphasizing nutritional counseling recommendations.

Hypoglycemia means low blood glucose. It usually occurs in discrete attacks with the symptoms of sweating, shaking, palpitations (adrenergically mediated), paresthesis, confusion, mental anxiety, and sometimes neurological signs (Table 24-14).[91] In classifying hypoglycemia it is important to distinguish reactive hypoglycemia from fasting, alimentary, and pre-diabetic hypoglycemia.

Table 24-14 Signs and Symptoms of Hypoglycemia

Adrenergic	*Neurological*
Palpitation	Headache
Sweating	Mental illness
Anxiety	Fatigue
Hunger	Confusion
Tremor	Amnesia
	Seizures
	Unconsciousness

From Permutt, M.A.: "Postprandial Hypoglycemia." *Diabetes* 25:719-736, 1976, p. 719. Used with permission of the publisher.

Neurological symptoms are usually predominant with gradual onset of fasting hypoglycemia. Adrenergic symptoms are usually associated with the more rapid onset of postprandial hypoglycemia. Both groups of symptoms, as well as either alone, may be observed in postprandial hypoglycemia.[91]

Fasting hypoglycemia is usually caused by insulin-secreting tumors, hormone-deficiency states, or alcohol and/or drug abuse. Alimentary hypoglycemia is associated with gastric surgery and may be due to rapid gastric emptying and/or excessive release of gastric inhibitory polypeptide (GIP) and other insulin-stimulatory gut hormones. Pre-diabetic hypoglycemia occurs in a small number of individuals who develop Type II diabetes. These patients should be monitored closely for the development of diabetes and are generally treated successfully with a diabetes diet.

Fasting Hypoglycemia

Fasting hypoglycemia not associated with diabetes is a potentially serious occurrence and is often caused by insulinomas or certain hormone-deficient states. It can be diagnosed by obtaining fasting blood sugars after a 12-hour fast and following three days of a high-carbohydrate diet (i.e., 250 gm carbohydrate/day). It has been reviewed in detail by Fajons.[92]

Alimentary Hypoglycemia

Alimentary hypoglycemia can occur in patients following gastric surgeries such as gastrectomy, gastrojejunostomy, or vagotomy and pyloroplasty. Symptoms usually occur two to three hours after eating. Leichter, et al., performed oral glucose tolerance tests on 16 post-gastrectomy patients and found nadir plasma glucose concentration of less than 50 mg/dl in 14 patients with symptoms described in eight.[93] The etiology of hypoglycemia appears to be rapid gastric emptying, since there is a close correlation of hypoglycemia with peak insulin levels and peak plasma glucose levels. Insulin secretion appears to be significantly greater in postgastrectomy patients with hypoglycemia than in those without hypoglycemia. Hyperglycemia has been shown not to be the cause of the hyperinsulinemia *per se*, and it has been hypothesized that excessive release of gastric inhibitory polypeptide (GIP) and/or other gut hormones that stimulate insulin release potentiates glucose-stimulated insulin release.[94] In fact, GIP hypersecretion has been implicated as a factor in the development of symptomatic postprandial hypoglycemia and delayed hyperinsulinism in patients without gastrointestinal disorders or surgeries.[95]

Early Diabetic Hypoglycemia

A third type of hypoglycemia has been referred to as early diabetic spontaneous hypoglycemia. Although this is an uncommon finding in the general population of Type II diabetics, it is a more common cause of hypoglycemia as compared to the other types.[91,96] These patients can be distinguished from idiopathic reactive hypoglycemics through use of the following criteria[96]:

1. Normal or slightly elevated fasting blood sugar—patients who have a fasting glucose above 130 mg% have not been shown to develop hypoglycemia;
2. slow postprandial glucose ascent with a zenith glucose greater than 150 mg%;
3. persistent hyperglycemia followed by a gradual fall to hypoglycemia levels between three and five hours after oral glucose;
4. symptoms are mild and transitory, and plasma glucose nadirs are generally higher than in reactive hypoglycemia; and
5. a family history of diabetes present in about 45% of patients.

Patients who generally fall into the above criteria should be monitored closely for development of diabetes. Treatment includes a diabetes diet. Occasionally the use of oral sulfonylureas has proven beneficial in normalizing glucose tolerance, possibly through the partial restoration of the sensitivity of the pancreatic beta-cell to normal physiological signals.[91] It is interesting that hypoglycemic early diabetics and non-hypoglycemic early diabetics have not been shown to differ in their patterns of insulin secretion, yet one group develops hypoglycemia and the other does not. It is possible that catecholamine responses between groups are different or that the hypoglycemic group has hypersecretion of gut insulinotropic hormones such as GIP. This theory has not been studied to date.

Idiopathic Postprandial Hypoglycemia or Symptomatic Postprandial Hypoglycemia

Idiopathic postprandial hypoglycemia is very difficult to accurately diagnose because of the many problems with the chemical criteria, including lack of diagnostic nadir glucose levels, overlap of chemical signs in the normal popula-

tion, variability of counter-regulatory hormone levels, and the vagueness of symptoms.

Reactive hypoglycemia has been misdiagnosed so often in recent years that some investigators and clinicians have coined the term "nonhypoglycemia" to describe those individuals who complain of fatigue, irritability, shakiness, diaphoresis, and other symptoms several hours after eating.[97] Often when these individuals are thoroughly studied, other disorders such as depression or anxiety reactions are the cause of their complaints. Johnson, et al., studied the Minnesota Multiphasic Personality Inventory (MMPI) scores of 192 patients who were being evaluated for hypoglycemia. They found that there is a high incidence of emotional disturbances, such as displacement of emotional problems to the soma, and depression in patients referred for evaluation of hypoglycemia; but there is no evidence that emotional disturbances can be ascribed to hypoglycemia.[98]

Whenever hypoglycemia has been investigated in detail, comparing various criteria, such as nadir plasma glucose following oral glucose tolerance tests, rate of drop in plasma glucose, and presence of symptoms at time of nadir glucose levels, the percentage of individuals meeting the criteria for hypoglycemia, as compared to those complaining of the disorder, is very small (i.e., 5-18%).[91,98,99]

Permutt, in a 1976 comprehensive review of hypoglycemia,[91] concluded that diagnosing clinically significant reactive hypoglycemia in any individual is difficult for the following reasons:

1. The oral glucose tolerance test is a poor reproduction of usual life events because of factors such as different composition of meals, emotional factors, activity levels, and ingestion of alcohol. Reactive hypoglycemic patients experience symptoms in real life after eating food; therefore, the significance of a "positive" oral glucose tolerance test remains uncertain.
2. There is no clear-cut distinction between a normal and a hypoglycemic glucose tolerance test. About 25% of normals have plasma glucose concentrations of less than 55 mg/dl without symptoms, but fewer than 8% have plasma glucose of less than 50 mg/dl when frequent samples are obtained.[99]
3. There is no current evidence that rapid decreases in plasma glucose produce clinical symptoms of hypoglycemia in the absence of chemical hypoglycemia.
4. The diagnosis of postprandial hypoglycemia does not exclude the coexistence of psychiatric disease, nor is the reverse true.
5. The etiology of alimentary hypoglycemia in the absence of gastric surgery, early diabetic hypoglycemia, and idiopathic postprandial hypoglycemia is unknown at present.
6. Diet therapy appears to be the most effective form of treatment on the basis of 40 years of experience. It would appear that the type of carbohydrate (starches rather than simple sugars) used in the diabetic diet and frequent small feedings may be the major elements in the effectiveness of this therapy.[91]

Since this review, several investigations have been conducted to further define the best criteria for the accurate diagnosis of reactive hypoglycemia. It is generally accepted that chemical criteria for hypoglycemia after ingestion of oral glucose (i.e., nadir plasma glucose below 50 mg/dl) have not been standardized or widely accepted.[100] Other suggestions of criteria for objective diagnosis include the occurrence of a rise in plasma cortisol greater than 20 ug/dl after symptomatic hypoglycemia.[101-103] Other subjects had increases in plasma levels of cortisol in association with blood glucose nadirs greater than 50 mg/dl. These obervations place into question the specificity of increased cortisol levels as a criterion for reactive hypoglycemia.

Since a rapid drop in blood glucose has been known to stimulate catecholamine release, Hadji-Georgapoulos theorized that the drop in blood glucose during a 90-minute period before reaching the nadir provided a better diagnostic criterion for symptomatic hypoglycemia than did the glucose nadir alone. High insulin levels 90 minutes before the glucose nadir were common in symptomatic subjects and correlated well with the hypoglycemia index he developed.[104] However, Johnson, et al.,[98] and Lev-ran and Anderson[99] were unable to separate those subjects with the symptoms of hypoglycemia at nadir glucose levels from those without.

It seems that all measures to date relating to the oral glucose tolerance test (namely, level of plasma glucose nadir, rate of glucose descent after reaching its peak, presence of hypoglycemic symptoms, and increase in cortisol levels) cannot be relied on singly or in concert for a diagnosis of reactive hypoglycemia. In addition,

insulin-glucose interrelationships in patients suspected of having reactive hypoglycemia are also heterogeneous.[105]

Since the oral glucose tolerance test is not the best diagnostic measure of reactive hypoglycemia, several investigators have recommended using a mixed meal with 250 to 300 grams of carbohydrate as the appropriate stimulus for evaluating symptoms and signs of hypoglycemia. Individuals who do experience symptoms during the three-hour test should subsequently be treated with appropriate dietary counseling.

If criteria are lacking for the accurate diagnosis of clinically significant hypoglycemia, what can the physician use to separate those few individuals who are truly symptomatic hypoglycemics from those whose symptoms are due to some other problem or problems? Since the oral glucose tolerance test contains more simple carbohydrates than the meals reputed to elicit symptoms, and since individuals with hypoglycemia complain of symptoms after eating meals or foods containing a mixture of nutrients, researchers have investigated whether individuals who have "chemical" hypoglycemia (plasma glucose nadir below 60 mg/dl after oral glucose tolerance test) experienced similar hypoglycemia and symptoms following a test meal of equivalent carbohydrate concentration.

Charles, et al.,[106] found that often after a mixed meal, no chemical hypoglycemia occurred in patients (mean plasma glucose 79 + 2 mg/dl); yet 14 out of 18 (78%) had symptoms or signs of hypoglycemia similar to patients following oral glucose tolerance testing. There was no significant difference in mean change in cortisol levels from basal, in mean basal insulin levels, rise in insulin levels, or certain glucagon and insulin levels between subjects and controls. The same was true for growth hormone levels. Mean plasma glucagon levels were significantly lower in patients than in controls at 180, 240, and 270 minutes after the mixed meal; glucagon secretion above basal was significantly lower in patients than in controls. The authors concluded that the signs and symptoms of hypoglycemia in symptomatic patients after a mixed meal were not due to the activation of the hypothalamic-pituitary adrenal axis. Nor could symptoms be related to the rate of change in blood glucose. Catecholamine levels were not measured in this study. Even though plasma glucagon levels were lower in subjects, plasma glucose levels were not significantly different. The authors concluded that subjects who have signs or symptoms suggestive of idiopathic postprandial syndrome in daily life be evaluated using a mixed meal as the stimulus, not by liquid oral glucose testing. For those rare individuals with symptoms, treatment should involve diet and counseling. Rarely should treatment involve drugs.

Hagan, et al., also compared the oral glucose tolerance test with a mixed meal in the diagnosis of hypoglycemia.[107] In addition to the parameters measured in Charles study,[106] Hagan, et al.[107] measured plasma norepinephrine levels and performed electroencephalograms (EEG) on 33 subjects referred for reactive hypoglycemia evaluation, plus 2 patients with insulinomas, and 36 normal volunteers. The composition of the mixed meal used in the study was 50% carbohydrate (1 gm carbohydrate/kg of body weight), 35% fat, and 15% protein. The typical meal consisted of 200 ml of orange juice, 2 eggs, 4 oz 2% milk, 20 gm cornflakes, 1 sl bread, 2 strips of bacon, 1 tsp sugar, 1 tsp butter, and 1/3 banana.

During the oral glucose tolerance test, 19 of the 33 subjects experienced symptoms of hypoglycemia, but they did not always occur concurrently with plasma glucose nadirs. Some patients did experience increases in plasma epinephrine concentration and pulse rate coincident with their symptoms. Nine subjects (27%) became symptomatic during the test meal but none had plasma glucose levels below 60 mg/dl, nor did they experience increases in catecholamine concentration or changes in EEG tracings. This would seem to refute the concept that the brain does not somehow receive sufficient glucose despite normal blood concentration.

Hagan, et al.,[107] agreed with Charles, et al.,[106] that on the basis of the oral glucose tolerance testing it is unlikely that hypoglycemia occurring after a meal is the cause of symptoms in many persons with hypoglycemia, and that the mixed meal is the procedure of choice in the evaluation of symptoms of reactive hypoglycemia.

Some researchers have found an increase in gut hormone levels, specifically GIP (gastric inhibitory polypeptide), in individuals with re-

active hypoglycemia. These hormones may be especially sensitive to sucrose and glucose in the diet and may be responsible for the delayed hyperinsulinemia observed in some patients.

A more recent theory as to the cause of symptomatic hypoglycemia following oral glucose tolerance testing relates cause to the observations by some investigators that these patients often have delayed hyperinsulinemia associated with a subsequent drop in plasma glucose following testing and development of symptoms. Hadji-Georgapoulos, et al., were able to show that hypoglycemic patients who had positive results during the oral glucose tolerance test did not demonstrate low blood glucose nadirs, delayed insulin peak, or symptoms following IV glucose testing.[108] Interestingly, the hypoglycemic patients had significantly higher GIP levels at zero, 60, 90, and 120 minutes during the oral glucose tolerance test as compared to controls. This led the authors to speculate that a gut factor(s) (i.e., GIP) is responsible for the delayed hyperinsulinemia of reactive hypoglycemia after glucose ingestion. It is possible that GIP-secreting cells are hypersensitive to glucose ingestion, and release excess GIP. Another study reported that normal subjects ingesting a diet of 30% sucrose had significantly higher postprandial GIP release than an isocaloric diet containing 30% of the calories as whole wheat.[109] It is possible that in postprandial hypoglycemic patients, elimination of sucrose from the diet could have an effect similar to that in normal subjects and could account for the absence of hypoglycemia after ingestion of mixed meals.[106]

Treatment

In general, studies on the treatment of postprandial hypoglycemia lack objective criteria for determining the effectiveness of the therapy. No studies have compared a treatment modality vs. placebo, and controlled clinical trials of various drugs used for postprandial hypoglycemia have not been performed.

Dietary Therapy

Although dietary therapy has been the treatment of choice for the past 40 years, few studies have been reported on this treatment. Therefore, many of the dietary recommendations have been based on anecdotal observations and influences derived from theories regarding the etiology of the disorder. Also, in most of the dietary studies performed, objective criteria for the diagnosis of symptomatic hypoglycemia were not applied; therefore, subjects may not have been true reactive hypoglycemics.

Anderson and Herman studied seven patients with "reactive" hypoglycemia and normal controls by placing them on a low-carbohydrate, high-protein diet.[110] They found that carbohydrate restriction further impaired carbohydrate tolerance in the hypoglycemic patients and did not provide symptomatic improvement. They suggested that hypoglycemic patients not be treated with carbohydrate-restricted diets but with a diabetic-type diet (i.e., low in simple sugars and higher in complex carbohydrates) as well as frequent feedings.[110]

Permutt, et al., studied the effects of carbohydrate restriction on the hypoglycemic phase of the oral glucose tolerance test in normal individuals.[111] They found that an isocalorically low carbohydrate diet (0% carbohydrate, 38% protein, 62% fat) followed for three days prior to an oral glucose tolerance test caused an alteration in glucose metabolism similar to that seen in early diabetic reactive hypoglycemia (i.e., delayed insulin secretion), followed by increased insulin secretion at 3-4 hours; hyperglycemia; and subsequent hypoglycemia (mean nadir glucose of 48 mg/dl) at 3-5 hours. The authors concluded that all oral glucose tolerance tests should be preceded by three days of a high-carbohydrate diet (i.e., 250 to 300 gm carbohydrate daily) to avoid false positive test results. Also, low-carbohydrate, high-protein diets often recommended for the treatment of hypoglycemia could actually provide hypoglycemic symptoms in normal individuals and could aggravate such symptoms in reactive hypoglycemics whenever they consume a high-carbohydrate food.

Other objections to the low-carbohydrate (less than 100 gm/day), high-protein diets recommended in the past are that the diets are usually also high in fat and that such diets might be atherogenic in susceptible individuals. The high-fat, frequent-feedings regimen can also promote excessive weight gain.

Dietary therapy is the treatment of choice for individuals with postprandial symptomatic hypoglycemia. A diet similar to the diabetic diet, restricted in refined carbohydrates, containing three regular meals per day, and between-meal feedings as necessary, appears to be the best

tolerated and most successful method of treatment for most hypoglycemic individuals.

From the limited research available, it seems more appropriate to limit the source of the carbohydrate rather than the total amount of carbohydrate in the diet (i.e., limit foods high in simple sugars, such as sucrose, honey, and corn syrup, and provide complex carbohydrates, such as breads, cereals, and pasta). Fructose, though a simple sugar, and foods high in fructose, might not pose a problem to hypoglycemic individuals. Crapo, et al., found this sugar did not promote hypoglycemia signs or symptoms in subjects with reactive hypoglycemia as compared to oral glucose.[112,113]

In the only recent study on the dietary intake of individuals with reactive hypoglycemia and related effects of dietary modification, Sanders, et al., found that the major correlative factor to providing relief of symptoms of hypoglycemia was the decrease in the refined carohydrate content of the diet and that restriction of total quantity of carbohydrate is of lesser importance.[114] Also, patients complied poorly to the 100-gm, low-total-carbohydrate diet and better to a diet restricting only simple sugar intake. Crapo, et al. also recommended close dietary follow-up to assure understanding and compliance to the diet.[112] The researchers did not recommend six equal feedings since subjects had improvement of symptoms by merely restricting refined carbohydrate, and symptoms returned when foods containing refined carbohydrates were added. Unfortunately, placebo effects were not controlled in this study.

Because of the varied dietary preferences in the population, no universally accepted dietary prescription can be applied to all patients with symptomatic reactive hypoglycemia, and recommendations must be tailored to cope with variations in dietary habits of patients. Often individuals with reactive hypoglycemia are advised to avoid alcohol and abstain from caffeine.[112] However, not one example of postprandial hypoglycemia secondary to these compounds has been demonstrated, nor has alleviation of hypoglycemia been shown by abstinence, aside from uncontrolled statements about improvements in patients.[91] Ethanol has been shown to potentiate glucose-induced hypoglycemia during an IV situation, but whether it potentiates postprandial hypoglycemia following mixed meals or in some susceptible subjects is unanswered. Other recommendations are often reported in the popular press for relief of hypoglycemia; they include multi-vitamin and mineral supplementation, especially with vitamin B-complex supplementation, consumption of unrefined and "natural foods," and avoidance of all dairy products. These recommendations are totally unfounded and are not based on any reproducible or reliable data. People who improve on such regimens usually do not have reactive hypoglycemia to begin with and are responding to a strong placebo effect based on the strong belief that a change in diet will help improve their "symptoms."

Utilizing the research information currently available, the following general dietary guidelines are recommended for those rare individuals who exhibit signs and symptoms of hypoglycemia following a mixed-meal tolerance test:

1. Restrict the intake of refined carbohydrate in the diet, specifically sucrose, glucose, and foods high in the content of these sugars. Since individual balances will vary as to the amount of sugar necessary to provoke symptoms, if sweets are consumed they should be done so with a meal rather than alone to blunt the insulin response and to delay gastric emptying.
2. Since fructose and lactose do not appear to have as dramatic a glycemic response, foods containing these sugars, such as fruits, dairy products, and foods sweetened with fructose, may be better tolerated in these patients.
3. The diet should not be restricted in complex carbohydrates, and an amount similar to the diabetic diet (i.e., 45-50% of total calories) is recommended. Foods high in fiber content, especially whole grain cereals and breads, are encouraged.
4. An individual who is overweight should be encouraged to reduce to a more reasonable weight to improve glucose tolerance.
5. Protein intake should approximate the average diet; i.e., about 15% of the total calories. Very-high-protein diets are not necessary and are often very high in fat content. High-protein low-fat foods include skim or low-fat milk products, poultry, lean meats, fish, dried beans, and dried peas.
6. The patient should be encouraged to eat three balanced meals per day; between meal feedings may or may not be necessary, depending on

activity levels and individuals' symptoms. Often an afternoon and bedtime snack will improve symptoms. The snack may be as light as a piece of fruit in the afternoon and a serving of starch and protein in the evening.

7. If the patient is a heavy user of alcohol and caffeine, consumption should be limited. For the occasional user, consumption on an empty stomach should be discouraged. Coffee or alcohol with a meal may be tolerated without ill effects.
8. In patients with hypoglycemia associated with the early stages of Type II diabetes mellitus, a beneficial effect has been reported with the use of sulfonylureas, possibly through the restoration of the sensitivity of the pancreatic beta cells to normal physiological signals.

Summary

True postprandial hypoglycemia in the absence of gastric surgery is a rare and often misdiagnosed condition. Symptoms similar to those experienced during a hypoglycemic episode can be attributed to a variety of emotional and physical conditions, including panic attacks, anxiety reactions, and depression. Accurate diagnosis is essential before treatment is initiated. Readjustment of lifestyle habits, such as poor eating routines, including numerous skipped meals, excessive alcohol and coffee consumption, and reduction of stress, will often go a long way to improve health and well-being in these individuals. If more serious emotional problems are present, psychological counseling may be recommended. For those individuals who exhibit symptoms during a glucose tolerance test following a mixed meal and during their daily lives, implementation of appropriate dietary measures usually provides satisfactory relief of symptoms.

Does Diet Prevent or Modify Juvenile and Criminal Behavior?

The 1984 prison release of Dan White, who killed San Francisco Mayor George Moscone in June, 1979, stimulated interest in the relationship of diet to criminal behavior and juvenile delinquency. The defense of Mr. White's behavior was that his compulsive diet of candy bars, cupcakes, and Coke was evidence of a deep depression and a source of excessive sugar that aggravated a chemical imbalance in his brain. The press called this the "Twinkie Defense."[115]

At present there is no valid scientific evidence to indicate that diet will cause a person to become involved in aggressive or antisocial behavior. The complex interaction between diet and behavior is difficult to investigate and will require numerous investigations measuring a variety of physiological as well as behavioral parameters.

There have been reports from corrections officials that restricting refined sugar, pasta, beans, rice, potatoes, milk, and other calorie-dense foods, such as soft drinks and candy, has improved juvenile behavior. However, these reports have been based on anecdotal observations, and at present there are no scientific studies to support these claims. Perhaps the personal attention given to the offenders has improved their behavior.[116,117]

The addition of megavitamins is also ineffective in improving behavior and may be harmful. Good nutrition is important for good health but does not guarantee "good" behavior. The individuals in correctional facilities should receive a diet adequate in all nutrients.

At present there is no valid scientific evidence to indicate that a person's diet will cause one to break the law, and violent behavior is not a characteristic symptom of hypoglycemia. Many patients consider hypoglycemia a disease and describe various symptoms associated with their conditions. However, individuals who claim they have a low blood sugar to account for their complaints and need an afternoon snack high in carbohydrate to give them more energy may be describing some other medical problem. A thorough physical examination and explanation of laboratory findings may ease a patient's concern for an existing condition.[97]

If offenders believe that diet rather than the individual controls behavior, they may conclude that they need not take responsibility for their own actions. Also, if judges, juries, and attorneys believe there is a relationship between crime and diet, the consequences may be even more serious.

Evaluation

While much is known in the area of nutrition and its relation to neurological disorders and behavioral disorders, much more is speculation. As you complete the following evaluative activities, be cognizant that new information is appearing rapidly in this area. Discuss your responses with fellow residents, physicians, and nutrition specialists to assure you are making decisions and evaluating information on the basis of the most current information.

1. A portion of this module deals with the prevention of behavioral and/or neurological disorders through the promotion of proper nutrition during pregnancy. From the material presented, prepare a list of nutrition-oriented advice you would give your pregnant patients. Also prepare a list of markers you could use to identify patients who may not be following your nutrition advice.
2. Make arrangements to meet with a recovering anorexic and a bulimic patient. During that meeting, discuss with the patients the motivation behind their anorexic or bulemic behavior, its effect on their lives, and how they felt about their behaviors before and during treatment.
3. Pre-Menstrual Syndrome is a relatively common problem for which there exists limited evidence supporting dietary therapy. Examine the most current literature available to you on this topic, in addition to the material provided in this module, and develop a therapeutic approach you feel is appropriate for PMS.

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Appendix A

Health Problems and Related Nutritional Risk Factors

Health Problem	Nutritional Risk Factors
Pregnant Women	
Iron-deficiency anemia	Inadequate dietary intake of iron, failure to utilize iron supplements
Megaloblastic anemia	Inadequate dietary folic acid intake, failure to utilize folic acid supplements
Toxemia	Malnutrition,[c] dietary sodium restriction
Newborns	
Intrauterine growth retardation, low birth weight	Maternal malnutrition, inadequate weight gain during pregnancy, underweight prior to pregnancy
Fetal alcohol syndrome	Excessive maternal intake of alcohol and associated malnutrition
Some types of congenital anomalies	Vitamin and mineral deficiencies and toxicities related to oversupplementation
Infants and Children	
Growth retardation , underweight	Dietary inadequacies
Elevated serum cholesterol	Excessive total fat, saturated fat, and cholesterol intake
Dental caries	Excessive, frequent consumption of sweets, lack of fluoride
Iron-deficiency anemia	Malnutrition, inadequate dietary iron intake
Infection	Malnutrition
Obesity	Caloric consumption exceeds caloric need
Constipation	Low fiber intake
Adolescents	
Hypertension	Overweight, excessive sodium intake, low potassium intake
Underweight	Undernutrition
Obesity	Caloric consumption exceeds caloric need
Dental caries	Excessive, frequent consumption of sweets
Infection	Malnutrition
Iron-deficiency anemia	Early introduction of whole cow's milk malnutrition, inadequate dietary iron intake
Elevated serum cholesterol	Excessive total fat, saturated fat, and cholesterol intake

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Appendix B

Nutrition Assessment and Intervention Guidelines for Population Groups in Community Nutrition

Nutritional Assessment Components	Method	Risks and Problems Indicated	Intervention Guidelines	Referral Sources
Pregnant Women				
Anthropometric Weight for height	Use weight-for-height tables to determine prepregnant weight status	Prepregnancy underweight, overweight	Adjust recommended weight to higher-than-average gain for underweight women and lower-than-average gain for overweight women	
Prenatal weight gain	Plot prenatal weight gain on appropriate grid[a]	Inadequate or excessive rate of weight gain. Rapid gains may indicate fluid accumulation.	Adjust food intake and activity level to correspond with desired rate of weight gain. Attempt to separate fluid gain from tissue gain if edema develops. Salt restriction is not indicated for the treatment of physiologic edema.	Maternal and Infant Care Projects: prenatal care; WIC Program; food stamps
Biochemical Hemoglobin Hematocrit Urine analysis	Standard technique. Dip stick for ketones, sugar, and protein spillage.	Anemia, gestational diabetes, preeclampsia	Adjust dietary and supplemental iron intake; control blood glucose levels	
Clinical Obstetric history	Questionnaire	Short interval between pregnancies (< 1 yr) and nutrient stores depletion. Inadequate/excessive weight gain history may be repeated. Anemia history may indicate probable reoccurrence. Prior oral contraceptive use may increase prenatal need for folic acid and vitamins C and B_6.	Replete nutrient stores with adequate diet and supplements if required. Adjust diet to include rich food sources of iron, folic acid, vitamins C and B_6 as indicated. Provide anticipatory guidance on optimal rate of and total weight gain.	Title XIX Early Periodic Screening,Diagnosis, and Treatment Program: Maternal and Child Health Services: state and local health departments; private physicians.
Dietary Diet quality and quantity, caffeine and alcohol intake levels Existence of pica	Repeated 24-hour or typical day food recalls; 3-day food record assessments; computerized dietary analysis assessment from a record of food intake; food group intake assessment	Low or excessive nutrient intake levels; excessive consumption of alcohol and caffeine-containing beverages; ingestion of non-food items.	Adjust diet to include food sources of needed nutrients. Discuss possible effects of alcohol on the fetus. Provide caution about excessive (> 500 mg day) caffeine consumption.	

Appendix B (cont)

Nutrition Assessment and Intervention Guidelines for Population Groups in Community Nutrition

Infants and Children				
Anthropometric Height for weight Height for age Weight for age Head circumference (to age 2 yrs) Skinfold thickness	Beam balance scale (nude or lightly dressed), measuring board and nonstretch tape. Status using National Center for Health Statistics (NCHS) growth grids. Skinfold calipers using standardized technique and validated predictive equation or nomogram.	Undernutrition, malnutrition. Stunting, failure to thrive (height for age < 5th percentile). Severe malnutrition (above plus head circumference < 5th percentile or a significant drop in range on growth grid). Overweight, obesity (weight for height > 95th percentile), percent body fat > 95th percentile.	Refer and report cases of child abuse. Refer children and families to food assistance programs. Adjust dietary intake to increase weight gain, or stablize intake until overweight is compensated by increases in height. Adjust activity level.	Private physicians; WIC Program; Children and Youth Program; Services for the Handicapped; Regional Center for High-Risk Newborns; Title XIX; Head Start; Child abuse and neglect centers; food stamps; Commodity Distribution Program
Biochemical Hemoglobin Hematocrit Serum cholesterol	Standard technique	Malnutrition, anemia, elevated serum cholesterol (≤ 150 mg/dl)	Improve dietary iron intake, supplement with iron, reduce cholesterol intake, apply additional serum cholesterol lowering methods as indicated.	
Clinical Birth weight for gestational age	Beam balance scale, digital scale, reference standard	Intrauterine growth retardation, large for gestational age	Adjust feeding to meet nutritional needs based on gestational age and catch-up group potential. Rule out hypoglycemia in small and large newborns.	
Blood pressure	Monitor in children over 3 years of age	"Higher than normal" blood pressure	Weight management, reduction of dietary salt intake if excessive.	
Dietary Dietary quantity and quality Feeding development	Interview or questionnaire on food groups, food recall, or record analysis	Malnutrition, underweight, overweight risk. Abnormal development of feeding and motor skills.	Adjust dietary intake to meet nutrient needs. Progress toward normal feeding developmental milestones.	

Appendix B (cont)

Nutrition Assessment and Intervention Guidelines for Population Groups in Community Nutrition

Adolescents				
Anthropometric Height Weight Skinfold thickness	Beam balance scales, nonstretch tape, calipers. NCHS growth grids for boys and girls 3 to 18 years of age. Assess weight status using weight-for-height grid. Assess percentage body fat using a reference standard. Assess growth velocity using reference standard.	Short stature, underweight, overweight	Adjust dietary intake and activity level.	Prenatal care; WIC Program; Maternal and Infant Care Program; physical fitness program and recreational facilities
Biochemical Hemoglobin Hematocrit Serum cholesterol	Standard techniques	Malnutrition, anemia, elevated cholesterol	Adjust diet, iron supplementation as indicated	Physician, psychologist, or guidance center
Clinical Blood pressure Dental disease	Standard techniques	"Higher than normal" blood pressure, dental caries	Weight management, salt reduction, reduction in sticky sweets consumption	Drug treatment centers; Alcoholics Anonymous; Neighborhood health center.
Dietary Dietary quality and quantity	3-day food record, diet history (computerized nutrient analysis)	Malnutrition	Adjust diet to meet requirements	Adolescent clinics; nontraditional alternative health centers

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Appendix C

Federally Sponsored Food Assistance Programs for Pregnant Women, Infants, Children, and Adolescents

Program Offered	Purpose of Program	Administering Agencies
Food stamps	Assist families in providing nutritious meals	U.S. Department of Agriculture (USDA) Food and Nutrition Service (FNS) and state welfare agencies
Special Supplemental Food Program for Women, Infants, and Children (WIC)	Assist pregnant women, lactating mothers, and children ages 1 to 5 years in obtaining specified nutritious foods	FNS and state health agencies
Commodity Distribution Program	Encourage and maintain domestic consumption of commodities; prevent the waste of commodities	FNS
Food for Child Care Programs	Initiate, maintain, or expand the provision of free meals and snacks to children in participating child care centers	FNS, state educational agencies, and public or private nonprofit day care centers
School Breakfast Program	Provide a nutritious breakfast free or at reduced prices to needy children attending participating schools	FNS and state educational agencies
School Lunch Program	Provide free or reduced-price lunch to children attending participating schools. Safeguard the health and well-being of the nation's children and educate children about nutritious food habits.	FNS and state educational agencies

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Appendix D

Self-Help Groups for Treating Eating Disorders

ANOREXIA NERVOSA & RELATED DISORDERS (ANRED)
Box 1012
Grove City, CA 93433
Gene Ann Rubel, President
(805) 773-4303 (24-hour hotline)

ANOREXIA SELF-HELP GROUP
Las Encinas Hospital
Pasadena, CA 94307
Paul E. Laemmle, Psychologist

AMERICAN ANOREXIA NERVOSA ASSN. OF ATLANTA
3533 Kingsboro Road, NE
Atlanta, GA 30319
Ann Bradshaw, President
(414) 233-7058

ANOREXIA NERVOSA & ASSOCIATED DISORDERS (ANAD)
Suite 2020
550 Frontage Road
Northfield, IL 60093
Vivian Meehan, President
(312) 831-3438

ANOREXIA NERVOSA AID SOCIETY OF MASSACHUSETTS, INC.
P.O. Box 213
Lincoln Center, MA 01773
Patricia R. Warner, President
(617) 259-9767

BULIMIA, ANOREXIA, SELF-HELP (BASH)
Suite 206
522 New Ballas Road
St. Louis, MO 63141
(314) 567-4080

AMERICAN ANOREXIA NERVOSA ASSOCIATION
133 Cedar Lane
Teaneck, NJ 07666
John A. Atchley, M.D., President
Estelle B. Miller, M.S.W., Vice-President
(201) 836-1800

ALBANY-TROY SELF-HELP
21 Paul Holly Drive
Loudonville, NY 12211
Anne C. Wang, President
(518) 462-4583

CENTER FOR STUDY OF ANOREXIA NERVOSA
One West 91st Street
New York, NY 16025
William Davis, M.D.
(212) 595-3449

NATIONAL ANOREXIC AID SOCIETY (NAAS)
550 South Cleveland Avenue
Suite F
Westerville, OH 43081
(614) 695-2009

AMERICAN ANOREXIA NERVOSA ASSOCIATION OF PHILADELPHIA
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(Conducts a lot of research here)

Appendix F

Binge Eating Questionnaire

BEQ Form S1.1

Form S1 SC # ... ... (3 4) SID # ... ... (5 6 7 8 9)

1. TODAY'S DATE: .....

NAME: .....
Last First Middle Init.

LOCAL MAILING ADDRESS: .....
Street

.....
City State Zip

LOCAL TELEPHONE: (.....) .....
Area

2. YEAR in college (as 1, 2, 3, etc.): ..... MAJOR: ..... (10, 11)

3. SEX: Male ☐ 0
Female ☐ 1 (12)

4. DATE OF BIRTH: ...../...../.....

5. PRESENT AGE: ..... years (13-15)

6. What is your PRESENT WEIGHT? ..... lbs (16-18)

7. What is your HEIGHT? ..... ft ..... in (19-20, 21-22)

8. What is the LOWEST YOU'VE WEIGHED since reaching your present height? ..... lbs (23-25)

9. What is the MOST YOU'VE WEIGHED since reaching your present height? ..... lbs (26-28)

10. In your opinion, you are now (check one)
very underweight ☐ 1
underweight ☐ 2
average ☐ 3
overweight ☐ 4
very overweight ☐ 5 (29)

11. What was the most you have weighed during the past year? ..... lbs (30-32)

12. What was the least you have weighed during the past year? ..... lbs (33-35)

13. Do you get uncontrollable urges to eat and eat until you feel physically ill? NO ☐ YES ☐ (36)

14. Are there times when you are afraid that you cannot voluntarily stop eating? NO ☐ YES ☐ (37)

15. Do you make yourself vomit after eating too much? NO ☐ YES ☐ (38)

16. Do you feel miserable and annoyed with yourself after an eating binge? NO ☐ YES ☐ (39)

17. Have you ever had an episode of eating an enormous amount of food in a short space of time (an eating binge)? NO ☐ YES ☐ (40)

18. Do you consider yourself a binge-eater? NO ☐ YES ☐ (41)

Appendix F (cont)

Appendix F Binge Eating Questionnaire

Binge-eating and vomiting 705

19. In order to control your weight, do you use . . .

Diet pills	never	☐	0
	less than once every four weeks	☐	1
	1 to 3 times every four weeks	☐	2
	once every week	☐	3 (42)
	2 to 6 times every week	☐	4
	once every day	☐	5
	more than once every day	☐	6
Laxatives	never	☐	0
	less than once every four weeks	☐	1
	1 to 3 times every four weeks	☐	2
	once every week	☐	3 (43)
	2 to 6 times every week	☐	4
	once every day	☐	5
	more than once every day	☐	6
Diuretics or water pills	never	☐	0
	less than once every four weeks	☐	1
	1 to 3 times every four weeks	☐	2
	once every week	☐	3 (44)
	2 to 6 times every week	☐	4
	once every day	☐	5
	more than once every day	☐	6

Other? ..... (Please specify) How often? .....
(*Note:* If you use these aids for other reasons, please specify reasons.) (45, 46-47)

20. What is the average number of days between your episodes of binge-eating? (If never, leave blank) ..... days (48-50)

21. Have you ever vomited after eating? NO ☐ YES ☐ (51)

22. How frequently do you vomit after eating?

never	☐	0
less than once every four weeks	☐	1
1 to 3 times every four weeks	☐	2
once every week	☐	3 (52)
2 to 6 times every week	☐	4
once every day	☐	5
more than once every day	☐	6

23. Do you have any other type of eating problem? NO ☐ YES ☐
If 'yes', please describe the nature of the problem (on back). (53)

If you have any questions concerning this questionnaire, please contact the Eating Disorder Clinic at The New York Hospital-Westchester Division, 21 Bloomingdale Road, White Plains, NY 10605. (914) 682-9100.

From Halmi, K.A., et al.: "Binge-Eating and Vomiting: A Survey of a College Population." *Psychological Medicine*, 11:697-706, 1981, pp. 704-705. Used with permission of the publisher.

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**a page number followed by a "t" indicates a table; an "f" refers to a figure.*

Some Abbreviations Used in the Nutrition in Primary Care Series

ATP	adenosine triphosphate
c	cup
cc	cubic centimeter
CNS	central nervous system
FDA	Food and Drug Administration
gm	gram
IBW	ideal body weight
IU	International Units
kcal	kilocalorie
kg	kilogram
lb	pound
lg	large
MCV	mean corpuscular volume
MDR	minimum daily requirement
med	medium
μg	microgram
mEq	milliequivalent
mg	milligram
MJ	megajoule
ml	milliliter
oz	ounce
RDA	Recommended Dietary Allowances
RE	retinol equivalents
sl	slice
sm	small
Tbsp	Tablespoon
TPN	total parenteral nutrition
tsp	teaspoon
USDA	United States Department of Agriculture